Journal of the Indian Medical Association

VOL. XVII, No. 1 CALCUTTA OCTOBER, 1947

EARLY DIAGNOSIS OF MALIGNANT GROWTHS WITH A BRIEF REFERENCE TO THEIR INCIDENCE IN INDIA*

R. MAHADEVAN, M.S., F.R.C.S. (ENG.), F.R.C.S. (EDIN.),

Surgeon, Erskine Hospital, Madura.

The importance of early diagnosis of malignant growths will be obvious to every one and as such no apology need be advanced for the choice of the subject. It appears to me that the best way to introduce the subject is by a brief reference to the incidence of malignant growths in our country.

INCIDENCE

That malignant growth is very common in our country, as indeed it is all the world over, must be common knowledge to all medical men. It occurs in all races of mankind, civilized or uncivilized; it also occurs in all vertebrate animals, wild or domesticated, carnivorous or herbivorous. Cancer shows several common features—biological, clinical, macroscopical and microscopocal—in man and animals. (Gye & Hosford, 1936). While the great frequency of carcinoma is known to all, medical men do not probably all realise the magnitude of the incidence. In countries where reasonably accurate statistics are available the condition is proved to be appallingly common. Thus, in Great Britain it is estimated that more than 10 per cent of the people who reach the age of 35 eventually die of cancer (Statistical review for the year 1934 by the Registrar General). It has been said, and I think with a fair amount of justification, that statistics on Indian lives are so scanty and scrappy that reliance on them is bound to endanger one's conclusions (Minnoo-Masani). Even so, it need not be seriously doubted that malignant growth is a menace quite common in our country. The incidence of carcinoma, according to statistics published in Western countries rises steeply after 40 and increases with advancing years : it is greatest in old age, but owing to lower figures of population in the later decades, most cases of cancer appear to occur before the age of 60. However, in our country only a small proportion reach the age of 60 and beyond. The average duration of life in United Kingdom is 62, while in India it is 26. Can we then have at least the consolation that the majority of us do not live long enough to suffer from and ultimately die of cancer? No, I am afraid we cannot have even this melancholy consolation. More than mere age counted in years, it is the functional senescence of the affected tissues that seems to play an important part in the origin of cancer. Thus, among a race of people in whom the expectation of life is only 26, the tissues may be old at an early age. I realise that such arguments may be fallacious for various reasons. Thus for example, our average mortality is very high (22 per 1,000 of the population, the highest death rate in the world) and our expectation of life very low, mainly because of deaths due to preventible causes such as malaria, small-pox, dysentery, plague, filariasis, etc., and due to very high infant and maternal mortalities, which again are in the main preventible.

The point I want to make out is this : Unless statistics are collected from a very large series, we cannot have any exact idea as to the relative frequency of the disease. We must know the type of cases that occur, the organs affected, the age, the sex incidence, etc. There is reason to believe that the incidence in India, classified according to the viscera affected, is at variance in some important respects from the incidence in other countries. To judge the correctness or otherwise of these ideas, an attempt has here been made to classify available information. The biopsy reports on malignant growths from different representative institutions have been combined and classified—these have been obtained from various hospitals in widely different parts of this Presidency and nearby—Vizagapatam, Madras, Cuttack and Madura. Each of these institutions is known to tap cases from a large area all around.

No case without biopsy report has been included in the series. Even cases in which clinically the diagnosis was beyond any reasonable doubt, have not been included in the review without biopsy, as this is the only sure, if not infallible way of ensuring accuracy.

The following tables show the analysis :

TABLE 1—SHOWING ANALYSIS OF TOTAL CASES

	Total no. of cases	*% of total*	*Remarks*
Carcinomas ..	940	86·2	The ratio between the groups runs parallel to that in other countries.
Sarcomas ..	149	13·8	

TABLE 2—SHOWING SEX DISTRIBUTION

Carcinoma	940	Male	531	(56·6%)
		Female	409	(43·4%)
Sarcoma	149	Male	100	(67·8%)
		Female	49	(32·2%)
Carcinoma & sarcoma ..	1089	Male	631	(67·1%)
		Female	458	(32·9%)

*Read at the Scientific Section of the 23rd All-India Medical Conference, Madura, December, 1946.

TABLE 3—SHOWING ANALYSIS EXCLUDING CARCINOMAS PECULIAR TO MALES OR FEMALES AND TAKING INTO CONSIDERATION ALL OTHER CARCINOMAS ONLY

[530 (49·7%) came under this group (leaving 559 in the group peculiar to sexes)]

Males	367—69·2%
Females	163—30·8%

TABLE 4—SHOWING CARCINOMA PECULIAR TO SEXES

	Sex	*% of total cancer cases*	*% of all cancer cases in men*	*% of all cancer cases in women*
Males ..	177	18·8%	33·3%	..
Females ..	235	25%	..	55·4%

TABLE 5—SHOWING INCIDENCE OF CARCINOMA ACCORDING TO THE VISCERA AFFECTED AND THE SEX DISTINCTION IN EACH

Region affected	Male (531 cases) *No. of cases*	*Expressed in % of all carcinomas in male*	Female (409 cases) *No. of cases*	*Expressed in % of all carcinomas in female*	Male & Female together *No. of cases*	*Expressed in % of all carcinomas*
1. In the region of the mouth *i.e.* lip, check, floor of mouth, tongue, palate, jaw, gum	124	23·3	51	12	175	18·6
2. Male reproductive organs:	171	32·2	..	..	..	..
Penis	154	29	..	..	..	..
Testis	17	..	..	..	..	..
3. Female reproductive organs:	..	..	128	31·3	..	..
Cervix uterus	..	..	80	19·6	..	..
Body of uterus	..	..	12	..	..	..
Ovary	..	..	25	..	..	..
Vagina, clitoris etc.	..	..	11	..	..	..
4. Breast	6	1·1	107	26·2	113	12
5. Alimentary system:						
Stomach	21	3·9	12	2·9	33	3·5
Rectum	38	7·2	7	1·7	45	4·8
6. Urinary system	8	1·5	3	0·7	11	1·2
7. Skin and appendages	58	19·2	32	7·8	90	9·6
8. Secondary deposits in glands	32	..	15	..	47	..
9. Other organs	93	17·5	48	11·7	141	15
Total	563	..	424	..	987	..
10. Excluding sec. glands cases	531	56·6	409	43·4	940	..

Table 5 shows something very important to be taken note of : Carcinomas in the region of the mouth (175), of male reproductive organs (171), of cervix and vulva (91), breast (113), rectum (45), and the skin and its appendages (90), together account for 585 out of a total of 940 cases. All these above conditions require only the eye or the examining finger for a diagnosis, *i.e., fully 62·2 per cent of cases are obviously visible or within reach of the examining finger.* Yet, most patients put up with their discomforts for such a long time that by the time treatment is resorted to, the condition is so far advanced that cure in any sense is out of the question.

TABLE 6—SHOWING CLASSIFICATION OF SARCOMA AND ITS INCIDENCE IN THE TWO SEXES

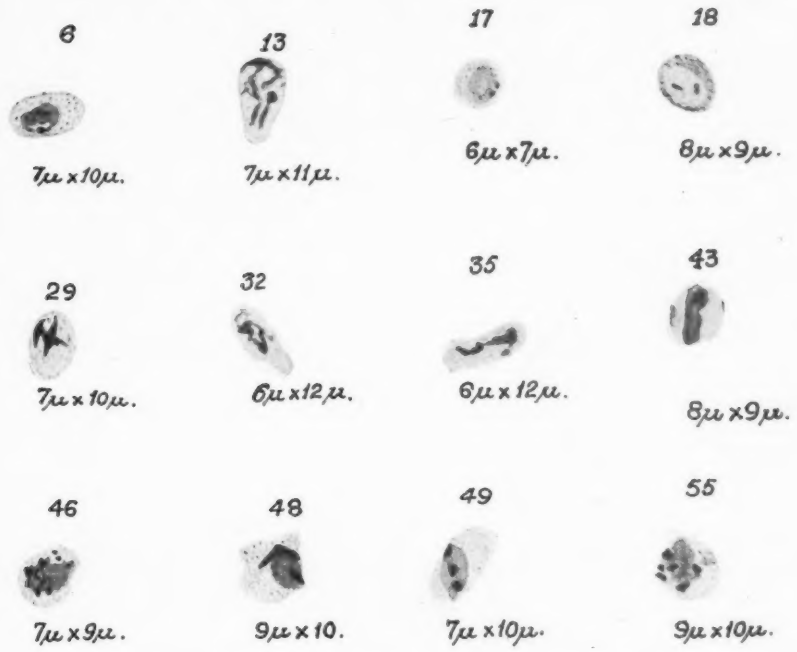
	Male	*Female.*
Fibro-sarcoma	29	12
Spindle-celled	15	12
Mixed celled	8	10
Endothelioma of bone	3	..
Ewing's tumour	4	..
Lymphosarcoma	19	4
Osteogenic sarcoma	6 (one in radius)	4
Reticulo-sarcoma	3	..
Neuro-sarcoma	4	2
Round-celled sarcoma	6	2
Myxo-sarcoma	..	2
Brain sarcoma (meninges)	2	..
Synovioma knee	1	..
Skin	..	1
Bladder	1	..
	100	49
Gand Total ..	149	

To draw inferences from the above tables may be erroneous for, a total of even 1,089 cases is too small a number for purposes of consideration of a disease of such great frequency as carcinoma. I have suggested a questionnaire (*vide* appendix) which, if sent not only to every member of the Indian Medical Association, but also to institutions and private bodies willing to co-operate in the work will, in the course of a few years yield an enormous amount of material from which accurate inferences can be drawn.

However, the above tables do bring out certain features which require comment and call for future verification. While the figures show that the proportionate incidence between carcinoma and sarcoma is the same as in other countries and incidence of carcinoma of the uterus, breast, larynx, etc., seem to correspond with the incidence elsewhere, some obvious differences are evident :—

Thus, carcinoma of the stomach seems to be far less frequent here. Of all types of cancer, our hospital statistics show the incidence of carcinoma of the stomach to be only about 3·5 per cent of the total, as against 22 per cent in Great Britain, 42 per cent in America, 55 per cent in Holland, Bavaria and Spain and 66 per cent in Czecho-slovakia. (Illingworth and Dick, 1935).

Again some statistics of other countries show a very large incidence of lung carcinoma. (Oschner A, and De Bakey, 1940). In these, the condition appears to be second to the stomach alone in the order of frequency. Thus, in Scotland, the total deaths, from pulmonary cancer in the year 1940 was 559 (Robertson, 1945). Maxwell (1935) says that accord-



Twelve representative drawings of Plasmodium Ovale from a Series of 58.

TYAGI—*Plasmodium Ovale Infection in U.P.*

FIGS. 1 and 2—An advanced case of malignant growth of the right maxilla (A.P. and lateral views).

FIGS. 3 to 5—A case of carcinoma of the breast in a male with a large secondary deposit in the skull (Figs. 4 & 5—A.P. & lateral skiagrams of skull).

N.B.—Biopsy report of the breast, as well as of the tumour scalp was "Adeno-carcinoma".

MAHADEVAN—*Early Diagnosis of Malignant Growths with a Brief Reference to their Incidence in India.*

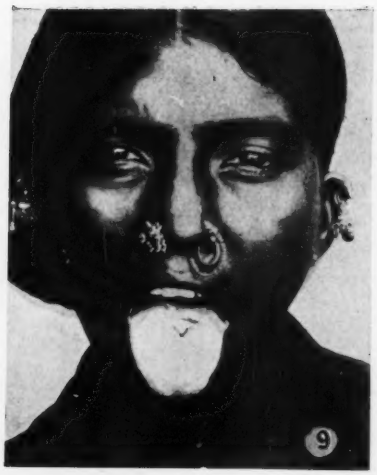


FIG. 6. (Case 3)—Advanced carcinoma of the breast in which almost the entire breast has disappeared.

FIGS. 7 and 8—Cases of carcinoma of the breast. At such a stage, it is obvious that cure is out of the question.

FIG. 9—Very early carcinoma of tongue—a hard nodule of the size of a match-head-in a young woman of 25, (confirmed by biopsy).

Engraved and Printed by
Bengal Autotype Co., Cal.

ing to most reliable statistics, carcinoma of the lung ranks next to carcinoma of the gastro-intestinal tract, breast and uterus. To quote Brock (1943) "Less than a generation ago primary carcinoma of the lung was thought to be a rare curiosity; today it is recognized as a common condition and ranks next to cancer of the colon in frequency in man". He sees on an average some 75 cases each year. Lung cancer does occur here, but it seems to be very infrequent. It cannot be that the condition is missed for want of proper diagnosis. If this was the case post-mortem records at least would show up some cases. Perhaps some racial peculiarity or a different environmental condition determines the frequency of a particular type of carcinoma in different parts of the world. Thus for example it is a general belief that tumours of the nasopharynx are uncommon, but this disease is particularly frequent amongst the Chinese at Shanghai and Hong-kong, as well as among the domiciled community in New York (Rao, 1944). Indeed *according to Digby and his associates (1941) tumours of the naso-pharynx rank, second in frequency in a list of all cases of malignant diseases.*

The story of malignant growths is a pitiful and depressing tale of "too late and too little"; "too late", as the patient in his ignorance reports for treatment when the condition is far too advanced for any treatment; and "too little" in results, as a direct consequence thereof. This seems to be the case, even in countries like America where facilities, both scientific and monitary, are so ample for an early diagnosis. In our country where facilities are as yet meagre and the people in the majority ignorant, medical help is sought only when the condition is far advanced.

Case Reports

Case 1—Figs. 1 & 2 show an advanced case of malignant growth of the maxilla. It is obvious that nothing can be done in these cases.

Case 2—Figs. 3 to 5 show a case of carcinoma of the breast in a male, with a big secondary deposit in the skull. Axillary glands of both sides were enlarged and hard. The patient had also hemiplegia of the right side, possibly due to the effect of secondary deposit in the brain. Biopsy report of the breast, as well as of the tumour of the scalp was, "adeno carcinoma".

Case 3—Fig. 6 shows a case of advanced carcinoma of the breast in which almost the entire breast has disappeared and there is extensive brawny oedema of the arm.

Figs. 7 and 8 show some more cases of carcinoma of the breast. In practice it is unusual to get cases earlier than these. If cases come at such a stage, it is obvious that cure is out of the question.

In the course of twentyone years in the profession and three years previous to that as a clinical student in the wards, I have seen few cases of early malignant growths. Indeed they have been so few that they are indelibly impressed in my mind. Thus, a young woman of 25 came complaining of a hard nodule in the tongue. It was practically the size of a match-head and was excised with a good amount of healthy tissue all around (Figs. 9 & 10) and submitted to biopsy. The condition proved to be carcinoma and required more extensive operation or radiotherapy; but the patient refused treatment and went home. Attempts at follow-up of the case also failed. In another instance, a man of about 50 came with evidences of rapidly developing pyloric obstruction. Operation showed an early growth in the pyloric antrum. Subtotal gastrectomy was performed and pathological report confirmed the condition to be one of carcinoma. There was no evidence of secondaries and indeed this was the one case in my series where the enlarged lymphatic glands were limited to supra and sub-pyloric groups.

As already mentioned, patients almost always come at an advanced stage of the disease due to their ignorance and poverty. Remedy for these involves large scale planning, improvement of social conditions etc., which are beyond the scope of this article. I propose to limit myself to the following, *viz.*, when a patient reports himself to the doctor very early in the disease, so early that diagnosis is in doubt, how can the doctor set about to settle the diagnosis?

Early Diagnosis

For this, first of all, I want to stress the following fundamental facts :—

1. The cause of cancer is still unknown. All that we do know is, that *cancer at its inception is a local disease. Even the most malignant tumour is localized in the beginning and at this stage it may be cured by excision through the healthy tissues around.*

2. Cancer in its early stage is painless. Pain indicates complication of some sort and often signifies a rather advanced stage. Pain may be due to ulceration infiltration, pressure on adjacent nerves, secondary deposits, etc. Consequently, if cancer is to be diagnosed early, one ought not to look for pain as one of the evidences.

3. Cancer does not arise in normal tissues. It arises in tissues already the seat of some pathological change, *e.g.*, leucoplakia of tongue; chronic ulceration; dental ulceration; chronic cholecystitis associated with gall-stones; renal stones and leucoplakia of renal pelvis; tears of cervix uteri; goitre; phimosis; etc., etc.

4. Cancer spreads by direct extension into the tissues around and through related lymphatic and blood vessels. To judge whether a growth is malignant or not, the relation of the tumour to the surrounding tissues is most valuable and *for this reason it is most important to examine the growing margin rather than the central part.*

5. Cachexia is a late symptom and one ought not look for it as an evidence of cancer, but must aim at a diagnosis long before any cachexia develops.

6. Text book descriptions are far from satisfactory. The majority of text-books still continue to give descriptions of carcinoma in very late stages. True, the importance of early diagnosis is mentioned,

but the early features are often indefinite, and consequently their descriptions are also vague, while the late features are definite and unmistakable. Graphic descriptions of these late stages are given which get fixed in the students' mind. Perhaps it will be wiser to omit descriptions of these late stages altogether.

7. The question of the age of the patient and duration of the disease should not unduly influence the diagnosis, *i.e.,* if other things point to a possible malignant condition, such a possibility should never be excluded merely because of the young age of the patient or long duration of the disease. I know of a case of carcinoma of penis which occurred in a child of two; carcinoma of the rectum at thirteen; oesophagus at twenty,—all verified by biopsy. Thus, once a question of malignancy arises, whatever the age or the duration verify with all the diagnostic aids, including biopsy, before a definite conclusion is arrived at.

Some Salient Features

The following illustrative case reports bring out clearly some salient features to be remembered.

Dental Ulcer and Malignancy—(*a*) A dental ulcer usually heals in about a fortnight after the extraction of the offending tooth. If it does not heal by that time, one should seriously review the condition and decide whether the ulcer is not associated with a malignant change. If on palpation of the margin of the ulcer, a hard nodule is felt, it makes the suspicion almost a certainty. This is so, even if the induration is over a minute spot only and the only way of settling the question is by a biopsy. Here a word about biopsy : Wherever possible the dental ulcer is better excised entirely together with a portion of the healthy tissue all around, and sent for biopsy. If the ulcer is too large for this procedure, tissues from two or three different places at suspicious spots must be taken along with the adjacent healthy tissue, particularly from places which feel hard.

May I add, here that one must get into the routine of *always* obtaining a pathology report on all tumours removed. To arrive at conclusions from naked eye appearances alone will lead to disaster sooner or later. Thus, a small nodule removed from the eye lid of a lady was found on a routine biopsy to be a hypernephroma. There was no suggestion whatever of any kidney trouble. On the basis of the pathology report alone the surgeon undertook an exploratory operation and detected an early hypernephroma of one of the kidneys and removed the kidney.

(*b*) Again, a hard nodule even of the size of a match-head in the margin of a gummatous ulcer of the tongue is a warning that the ulcer is turning malignant. Do not look for such conditions as difficulty in protrusion of the tongue, or of excessive salivation. Such signs are evidences of advanced infiltration fixing the tongue and interfering with the normal swallowing of saliva.

(*c*) If a leucoplakic patch of the tongue, lip or cheek becomes larger, thicker, or ulcerated, these are warning signs of transition to carcinoma.

2. Carcinoma of the Breast—*In a middle aged woman, lump in the breast felt with the flat of the hand is likely to be a carcinoma, in 9 out of 10 cases.* It is important to palpate with the flat of the hand and not pick up the breast substance with the tips of the fingers. In the latter way many nodules may be apparent which are not pathological and a significant hard lump may be missed. Such early signs as elevation or deviation of the axis of the nipple (even in the absence of retraction of the nipple) have great significance and can be appreciated only by comparing with the normal breast. This is possible by examining the patient in a good light, in sitting posture, with the clothes taken off the chest. Some patients are unwilling to be examined thus, even by a lady doctor. Imperfect and partial examinations of the breast in a shy patient will only result in missing an early growth. If the patient is shy, it is far better to refer the case to a lady doctor and in any case it is wise to refuse to give an opinion unless complete examination is allowed. It is interesting to quote here Bradfield's (1930) observation. He states, "Formerly we have commented on the comparative rarity of cancer of the breast, but during the past year this belief has been upset, and suggests that there is a tendency for women to conceal the disease. The statistics bear out what has been reported before, that the incidence of the disease is very much the same in India as it is in other parts of the world."

Incidentally, it is worth while remembering that if a lump is felt, but one is not sure whether it is a tense cyst or a solid substance, transillumination of breast may help. It may show up a cyst clearly, but where a cyst is present, it is unwise to be satisfied with tapping a cyst. It is far better to excise it and examine it carefully, because the cyst may be the result of obstruction to the duct by an early growth.

Where a lump is felt, but the diagnosis is in doubt, it is better to excise the lump together with the healthy tissue around with diathermy knife and submit to biopsy report. Indeed, if at all there is reasonable evidence of malignancy and if the patient is willing, a simple excision of the breast should be done. If there is report of malignancy, a radical excision must soon follow. Some delay is inevitable in adopting these methods. To obviate this, the method of frozen section may be adopted, but this requires a trained pathologist who has wide experience with the interpretation of frozen sections. In general it may be said that *it is advisable to make the diagnosis from examination of the primary growth alone and let the condition of the lymph nodes help in determining prognosis.*

3. Carcinoma of Stomach—Mere loss of weight and general debility may be the only symptom. Indeed in a middle aged patient, where an obvious cause (*e.g.,* tuberculosis, anæmia due to ankylostomiasis etc.) is not found to explain such symptoms, the possibility of carcinoma of the stomach must be seriously considered and every test must be applied to exclude or confirm the diagnosis.

Achlorhydria or hypochlorhydria need not be present. Hypochlorhydria is the result of gastritis rather than directly of the cancer. Patients with gastric cancer may be found to have free hydrochloric acid. (Keynes, 1946). In many of Jussawall's cases a high free and total acidity was present, one case even showing a free acidity of 167 in the fasting juice (Jussawall's, 1947).

Place of Diagnostic Laparotomy—Where the various examinations leave one in doubt, it is the duty of the doctor to advise a diagnostic laparotomy. This is perfectly justifiable and *it is far better to do it and find no growth than to wait and watch.* If the latter course is adopted, it will be found that by the time the conditions becomes definite, it has also become inoperable.

4. Piles and Carcinoma Rectum—A patient may come with the complaint of bleeding per rectum. If proctoscopic examination in such a case shows hæmorrhoids, it does not necessarily exclude a more serious condition above. Carcinoma of the rectum may exist without any more evidence than bleeding during defæcation, from piles as a result of interference with venous return by the growth at a higher level. *In no case should piles be treated as such in a middle aged or elderly patient without a routine sigmoidoscopic examination.* Indeed, patients have come to hospital after operation done elsewhere for piles. They came because their symptoms had not improved. A digital examination in some of the cases has shown an obvious malignant growth low down and easily accessible to the examining finger and one wonders how the condition could have at all been missed, if a rectal examination had been done prior to operating on the piles.

Rectal examination is one of the simplest and yet one of the most sadly neglected procedures. Many a growth in rectum could easily have been diagnosed, weeks if not months earlier, if only the doctor had not neglected this simple but one of the most important of methods.

Digital rectal examination is useful not only for locating growths in rectum, but also growths higher up. With the patient sitting and a finger in the rectum many a growth at the pelvi-rectal junction and in the pelvic-colon nearby may be felt. In some cases, with a finger in the rectum and a palpating hand on the lower abdominal wall of the recumbent patient, a pelvic-colon growth may be detected—by bimanual palpation. In yet others, instead of having the patient on the back or turned to left side as is often done, if the examination is done with the patient turned to the right (Abel's position), a growth in the fundus of the pelvic-colon, not palpable otherwise, can be felt: for, in this latter position, the weight of the growth brings the fundus of the pelvic-colon nearer to the palpating finger, while in the other position it takes the growth away from it. Thus, by such simple methods, a growth can be diagnosed with an amount of certainty, which may not be available even by barium enema or by sigmoidoscopic examination.

A word about stool examination—The mere evidence of chronic bacillary or amœbic dysentery does not necessarily exclude carcinoma. Indeed, where an ulcer is felt in the rectum and at the same time amœbæ are found in the stool, if quick response to emetine injections is not obvious, it is wise to take a biopsy from selected areas of the ulcer margin. *Dysentery may be superimposed on a carcinomatous condition* and this point should always be borne in mind.

5. Other Examples—(a) *Brain Tumour*—One cannot go into details here but I want to stress on one feature *viz.*, the significance of localized headache. I quote the following: "Localized headache sometimes appears as an early symptom without evidence of increased intracranial pressure. A superficial tumour of the brain may cause localized neuralgic pain, usually associated with tenderness. The meningiomas are especially apt to produce this symptom, and it is seldom absent when the tumour invades the skull. Tumours of the posterior fossa, especially those in the neighbourhood of the foramen magnum, often produce pain in the suboccipital region and back of the neck as an early symptom. Associated with this there is sometimes localized tenderness, and some degree of cervical rigidity. The pituitary adenomas are apt to cause bitemporal or bifrontal pain of a boring character and often severe" (Symonds and Cairns, 1936).

(b) *Carcinoma of Larynx*—It forms about 2 per cent of all carcinomas in other countries and seems to be of similar frequency in our country also. In a middle aged or old person, a hoarse voice or change in the voice not due to any ascertainable cause and not clearing up in three weeks by ordinary methods, may be due to carcinoma larynx and every method of examination must be adopted before the condition is confirmed or ruled out. *It is all the more important to diagnose this condition because in no other region of the body are the chances of permanent cure of cancer by surgery more hopeful than in this condition* (Rao, 1941, 1944, 1945). The same author deplores that the large majority of these patients come too late for any hope of cure.

(c) *Goitre becoming Malignant*—A goitre may become malignant several years after its existence, and the long duration of a goitre should not influence one *in negativing a possible malignant change.* Further, it cannot be too strongly emphasised that *contrary to general belief carcinoma of thyroid is often slow in its evolution.* Pain radiating to the neck and head, an increase in hardness or size of a nodule, dysphagia —all must be seriously treated as evidence of malignancy. Under such circumstances, it is far better to remove the thyroid gland than to wait and see.

(d) *Bronchial Neoplasms*—Unexplained cough or breathlessness may be the only early evidences of a bronchial neoplasm. Such cases must be investigated by bronchoscopy, lipiodol x-ray etc. At present, even in the best hands the actual operability rate is only about 8 per cent (Brock, 1943). With earlier diagnosis this figure may be improved upon.

(e) *Mole*—If a mole becomes larger in size or ulcerates or bleeds easily or becomes painful, think of the probability of its turning malignant.

(f) *Carcinoma Penis*—Urethral discharge in a phimotic prepuce has been treated more than once as gonorrhœa. The correct thing is to slit the prepuce and see and in doubtful cases biopsy from indurated areas must be taken. In fact in the majority of such cases, on slitting the prepuce, if a carcinoma is present, there are unmistakable evidences of it. *The condition is missed simply because so simple a procedure as slitting the prepuce and seeing the glans is not done.* Indeed, in such cases, palpation will give unmistakable evidences of it even before slitting. If there is a nodule or leucoplakic patch in the prepuce, it is best to circumcise and get a biopsy report of the suspicious areas. In cases with growth inside a phimotic prepuce there is often a characteristic dumb-bell shaped appearance of the glans which is unmistakable.

Place of X-Rays

While skiagrams may be of great help if properly interpreted, the findings from these should not ordinarily be allowed to exclude the diagnosis of a malignant growth, if clinical features point to such a probability. For example, the mere absence of a filling defect in barium-meal skiagrams should not exclude a carcinoma of stomach or colon, if clinical features suggest these conditions. *In such cases the next step must be by an exploratory laparotomy.*

Prevention of Malignant Growths

The supervention of malignant growths on certain pathological conditions, can be prevented, by what may well be called prophylactic operations. A timely removal of a leukoplakic patch of the tongue, extraction of a carious or irritating tooth or stump, early treatment of pruritis, vulvæ and leukoplakia of vulva (Watson and Gusberg, 1946), removal of goitres, excision of large moles, removal of gall stones and renal stones, prevention or proper treatment of chronic ulcers, proper treatment of tears of cervix uteri and erosions of cervix, circumcision of phimotic prepuce, removal of papilloma and adenoma in rectum or colon etc. will go a long way in the prevention of malignant growths.

Social Work

A large number of the poorer class of patients of both sexes in the area of Vizagapatam and other parts of Andhradesa are inveterate smokers. Leukoplakia and cancer of the hard palate are very much more common in women who smoke with the lighted end of the cigar inside the mouth, evidently to escape notice and the social stigma attached to smoking amongst women (Rao, 1944). Incidentally, the same author stresses on the relation of smoking to carcinoma of laryngo-pharynx. He says that the evidence is too strong, both experimental and clinical indicating smoking as an extrinsic factor of great importance. (Rao, 1941 and Flory, 1941). These examples suggest the line on which social work may be undertaken towards the prevention of malignant growths.

Conclusion

The conclusions in the main are as follows:—

(1) There is reason to think that while carcinomas are as frequent in our country as in other parts of the globe, there seems to be some important differences in the incidence as classified according to the viscera affected. These are fully discussed. A plea is made for collecting statistics on a much wider scale than now, so that reliable conclusions can be drawn.

(2) One of the few favourable features of even the most malignant tumour is their local origin and it is upon this that the whole treatment of cancer by surgery is founded.

(3) Fully 62·2 per cent of the growths occur in regions easily visible to the naked eye or accessible to the palpating finger.

(4) Omission of such simple examinations as a digital examination of the rectum or sigmoidoscopic examination is responsible for missing early recognition of at least some of the cases of carcinoma rectum, colon etc.

(5) Pain is not a feature of carcinoma anywhere, in the absence of complications.

(6) Such considerations as young age of the patient, very short or very long duration of the disease, negative x-ray findings etc. should not be allowed to exclude a malignant growth, if other features point to it.

(7) The place of exploratory operations for diagnostic purposes is discussed.

(8) Pre-cancerous conditions properly treated can go a long way in preventing incidence of malignant growths.

(9) At present, the majority of cases came too late to be benefitted by any treatment. The main reason for this is ignorance on the part of the patients. No improvement can occur until the general level of education, social condition etc. of the entire mass improves.

Acknowledgment

My thanks are due to the superintendents of the hospitals and staff of the pathology department of the institutions already mentioned. Particular mention must be made of my house surgeons, Dr. Miss. Kameswari, and Dr. Kotayya at Vizagapatam, Dr. Swaminathan at Erskine Hospital, Madura; also Dr. P. V. Jannadha Rao, Lecturer in Surgery and Surgeon at Cuttack Hospital. Many others helped me in this task, but the list will become inconveniently long to mention individually, and my grateful thanks are specially due to all of them.

APPENDIX

QUESTIONNAIRE FOR COLLECTING STATISTICS OF MALIGNANT GROWTH

1. Serial No.
2. Name
3. Sex
4. Age
5. Address
6. Occupation
7. Where treated
8. Disease
9. Duration
10. Pathological Report
11. Remarks

(*a*) Details of all cases where confirmatory biopsy reports are available, are requested in a tabular form as given above.

(*b*) Give separately details (similar to above) of cases which were clinically definite but no biopsy was done.

(*c*) In remarks column, mention any factors of importance, *e.g.* presence of phimosis in carcinoma of penis, any suggestion of occupational relationship to the disease, habits etc. *e.g.* smoking with burning end of the cigar inside the mouth in cases coming with cancer of palate.

(*d*) Wherever possible, please send clinical photographs, reprints of skiagrams, microphotographs of pathological sections etc.

REFERENCES

GYE, W. E. AND HOSFORD, J.—The British Encyclopaedia of Medical Practice by Sir Humphry Rolleston, 1937, Vol. II., p. 3737.

BRADFIED, E. W. C.—*Indian M. Gaz.*, **65**:426, 1930.

BROCK, R. C.—*Brit. M. J.*, **2**:1943.

DIGBY, K. H. AND OTHERS—*Brit. J. Surg.*, **28**:517-37 1941.

FLORY—*Lancet*, **2**:78, 1941.

GYE, W. E. AND HOSFORD, J.—The British Encyclopaedia of Medical Practice by Sir Humphry Rolleston, 1937, Vol. II., p. 737.

GREENWOOD, M.—*Cancer Rev.*, **3**:97, 1928.

ILLINGWORTH, C. F. W. AND DICK, B. K.—Text book of Surgical Pathology, 4th edition (J. & A. Churchill Ltd.) p. 467.

JUSSAWALLA, D. G.—*Indian J. Surg.*, **9**:8, 1947.

KEYNES, GEOFFREY—*Practitioner*, **15**:394, 1946.

KHANOLKAR, V. R.—*Indian J. M. Research*, **33**:2, 1945.

MAXWELL—*Brit. M. J.*, **1**:369, 1935.

NARASIMHA IYER, N. S.—*South Indian Med.*, **4**, Jan. 1938.

Idem—*J. Madras M. A.*, No. 1931 January, April, July, Novr., 1932.

OSCHNER AND DE'BAKEY, M.—*Surgery*, p. 992, 1940.

RAO, TIRUMAL, B.—*J. Indian M. A.*, **14**:1-7, 1944.

Idem—*Ibid.*, **13**:95-98, 1947.

Idem—*Ibid.*

Idem—*Medical Digest*, **9**:374, 1947.

ROBERTSON, C. K.—*Edinburgh M. J. May*, **6**:296, 1943.

SYMONDS, C. P. AND HUGH CAIRNS—The British Encyclopaedia of Medical Practice by Sir Humphry Rolleston 1937, Vol. II. p. 619-640.

Statistical Review by the Registrar General of Great Britain, 1934.

WATSON, B. P. AND GUSBERG, S. B.—*Am. J. Obstet. & Gynec.*, **52**:179, 1946.

ON THE CHEMISTRY OF ANTACIDS

SUDHAMOY MUKHERJEE, M.SC.,

From the Bengal Immunity Research Laboratory, Calcutta

Antacids are substances used in medicine for the neutralisation of gastric acidity. Hydrochloric acid is a normal constitutent of gastric juice and its presence enables pepsin, another constituent of the same, to digest proteinous food materials. The concentration of hydrochloric acid in the freshly secreted juice (Starling, 1936) is 0·5 to 0·6 per cent (0·138 N to 0·165 N). But the strength of the acid is reduced by reaction with (a) mucus which is secreted along with gastric juice, (b) proteins derived from food and their digestion products, and (c) alkaline substance of the duodenum which is regurgitated through the pylorus. Reduction of its strength is also effected by dilution with the liquid taken along with the food. The resulting concentration is variable, but analysis of normal chyme withdrawn for gastric analysis has been found to show 0·1 to 0·2 per cent. (0·027 N to 0·055 N) of the acid (Wiggers, 1934). Hyperacidity is generally caused by the deficiency of one or several of the factors which normally act to dilute or neutralise secreted gastric juice, or by such factors as increased rate of secretion of normal gastric juice and delayed gastric evacuation. In hyperacidity, the free acidity of the chyme approches that of the pure gastric juice, and the increased concentration of the acid often leads to irritation and spasm of the stomach muscles, commonly recognised as the familiar heart-burn and stomach pain. Hydrochloric acid at this concentration by itself has no harmful action on the gastric mucosa, but pepsin in the presence of about 0·1 N hydrochloric acid has a considerable destructive action, particularly on damaged or ulcerated tissues. In cases of peptic ulcer, the presence of acid not only causes irritation but inhibits the growth of the granulation tissue thereby delaying the process of healing. The administration of antacids is, therefore, frequently resorted to for relieving the distressing symptoms of hyperacidity as well as for controlling the acidity in the treatment of peptic ulcer.

Theoretically speaking, any substance which can neutralise hydrochloric acid, without being poisonous to the system, may be termed an antacid. But important differences exist between one antacid and another, *e.g.*, in the rapidity of neutralising action, in the pH to which it can raise the stomach contents, and in the physiological actions of the substances themselves as well as of the products of their reactions with the acid in the gastric juice and with the alkaline substance in the intestines. A clear understanding of the chemical, physicochemical and biochemical characteristics of the antacid substances is, therefore, of great importance for the proper choice of an antacid for specific cases.

SPEED OF NEUTRALISATION

The acid neutralising power of a substance is a function of its basic strength. Among the metallic compounds, the acid neutralising power generally fol-

lows the electropositive character of the metal. For this reason, alkalis (*e.g.*, sodium or potassium), as a rule, provide stronger antacids than the alkaline earth metals, (*e.g.*, calcium or magnesium), and the latter are again stronger than aluminium or bismuth. Oxides or hydroxides of metals are generally more reactive than the corresponding salts, and only salts of weak acids, which show little acidity in the free state, can function as antacids. An important factor governing the rate of neutralisation of an antacid, however, is its solubility in water, since the interaction takes place only in solution. For sparingly soluble substances, the available surface area determines the rate of solution, and the fineness of the powder is, therefore, of importance. The solubilities in water of a number of common antacid substances are given in Table I.

TABLE I—SHOWING SOLUBILITIES OF ANTACIDS

Substance	*Chemical formula*	*Solubility* *Parts per 100 parts of water*	*Remarks*
Sodium bicarbonate	$NaHCO_3$	6·9 at 0°C 16·4 at 60°C	
Calcium hydroxide	$Ca(OH)_2$	0·185 at 0°C 0·77 at 100°C	
Magnesium hydroxide	$Mg(OH)_2$	0·0009 at 18°C	Solubility products = 10^{-11}
Calcium carbonate	$CaCO_3$	0·0065 at 20°C 0·002 at 100°C	
Magnesium carbonate	$MgCO_3$	0·0106 at 0°C	
„ hydrate	$MgCO_3$, $3H_2O$	0·1518 at 19°C	
Bismuth carbonate	$Bi_2O_3CO_2.H_2O$	?	Practically insoluble in hot and cold water.
Aluminium hydroxide	$Al(OH)_3$	?	Solubility product = 10^{-33}
Aluminium phosphate	$AlPO_4$	?	Practically insoluble in hot and cold water.

Obviously, sodium bicarbonate should have a more rapid neutralising action than calcium or magnesium hydroxide, and the latter again more than aluminium hydroxide. The alkaline earth carbonates neutralise acid with moderate speed, but bismuth carbonate which can react with concentrated hydrochloric acid, does not practically react with the low concentration of the acid as present in the stomach.

pH OF NEUTRALISATION

When an antacid is added to hydrochloric acid, the pH of the solution gradually increases as the neutralisation proceeds, and the end-point of the reaction is indicated by a rapid rise in the pH. Fig. 1 contains curves showing the changes of pH of a 0·1 N hydrochloric acid solution consequent on the additions of varying quantities of a few typical antacids. These show that milk of magnesia [$Mg(OH)_2$] causes a steeper rise of pH at neutralisation than sodium bicarbonate, and renders the solution highly alkaline on the addition of even a slight excess. With magnesium trisilicate, the pH remains near about 6·0 after the addition of a considerable excess, but colloidal aluminium hydroxide raises the pH only up to 4·0 and maintains it at that level often after further additions.

Usually, the dose of an antacid is so adjusted as to leave an excess after neutralising the acid in the stomach. Since the actual quantity of the acid is variable, an idea of the conditions existing in the stomach after the administration of the antacid would be obtained by determining the pH of aqueous solutions or suspensions of antacids after the addition of varying amounts of hydrochloric acid. The curves obtained in this manner for a number of antacids are given in Fig. 2. The flat portions indicate the pH values of antacid-hydrochloric acid mixtures when the former is in excess. The pH levels for the different antacids are in the order :

$$Mg(OH)_2 > Mg_2Si_3O_8 > MgCO_3 > NaHCO_3 > CaCO_3 > Al(OH)_3 > Bi_2O_3.CO_2.H_2O$$

It should be remembered that the pH values were obtained after allowing sufficient time after each addition of acid for attaining equilibrium conditions, and therefore the consequences of differences in the rates of neutralisation are not evident from these curves. For example, magnesium trisilicate is known to be a slow-acting antacid (Mutch, 1936) and hence the pH of the solution immediately after each addition would be much lower than shown here. Aluminium hydroxide shows as before its characteristic buffer action near pH 4·0.

Doubt has however been expressed as to whether the neutralising actions of antacids as found by *in vitro*-experiments would correspond to these *in vivo*. Breuhaus and Eyrly (1941) concluded from determinations of the pH of stomach contents *in situ* by introducing a special glass electrode into the stomach that the degree of reduction of gastric acidity accomplished by an antacid cannot always be predicted from its potential neutralising power as determined by titration. They found that in most cases the increase of pH when determined *in situ* is surprisingly small. On the other hand, Rosette and Flexner (1943) observed with a continuously recording pH meter, both *in vitro* and in the human stomach, that both methods gave almost identical results. It seems probable that non-attainment of equilibrium between the antacid added

* Unpublished data from this laboratory.

and the whole of the acid contained in the stomach would lead to such discrepancies between the *in vitro* and *in vivo* experiments.

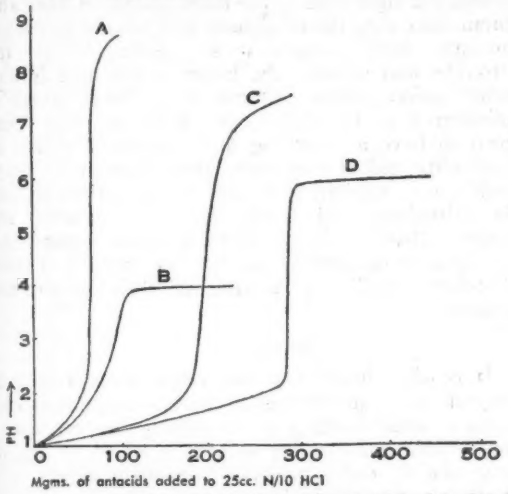


FIG. 1—A—Magnesium hydroxide. B—Aluminium hydroxide. C—Sodium bicarbonate. D—Magnesium trisilicate

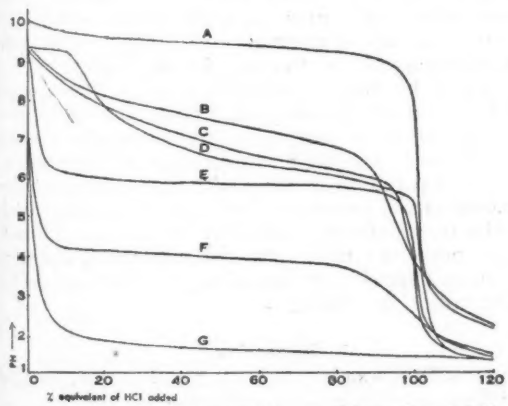


FIG. 2—A—Magnesium hydroxide. B—Magnesium trisilicate. C—Magnesium carbonate. D—Sodium bicarbonate. E—Calcium carbonate. F—Aluminium hydroxide. G—Bismuth carbonate

As the pH of the stomach juice can be raised to any degree by the addition of one or other antacid, it is for the clinician to decide on the type of antacid required according to the condition of the patient. It may be recorded here that complete neutralisation, *i.e.*, to pH 7·0, or raising the pH into the alkaline region is considered undesirable because such conditions stimulate further secretion of gastric juice, thus bringing back the original acid condition. Besides, the maintenance of an acid condition in the stomach is necessary for peptic digestion. On the other hand, Schiffrin and Warren (1942) showed from experiments on cat that the maximum destruction of tissues occurs at pH 1, but at a pH 2·24 pepsin has no such effect. Gill and Keele (1943) stated that pepsin would be incapable of damaging an intact or damaged mucosa in man at pH 3·5 to 4·0. It is now being generally accepted that a pH of 3·5 to 4·0 would be harmless to the ulcerated tissues and would at the same time provide a sufficiently acid medium for peptic digestion to proceed.

Having decided what pH is the most desirable, the problem remains, how to attain this in practice. It would be seen from the curves in Fig. 1 that for neutralising 25 c.c. of a 0·1 N hydrochloric acid to pH 3·5, the quantities of different antacids required are : $Mg(OH)_2$—60 mgm; $Al(OH)_3$—102 mgm; $NaHCO_3$—198 mgm; and $Mg_2Si_3O_8$—288 mgm. But if the quantity of the antacid added be in excess of these amounts by only 10 mgms, the pH of the solution would be: $Mg(OH)_2$—7·6; $Al(OH)_3$—3·9; $NaHCO_3$—5·9; and $Mg_2Si_3O_8$—5·85. This shows that except for aluminium hydroxide, the dose of the antacid would need accurate adjustment in order to bring the stomach pH to the designed level. But this presupposes a knowledge of the exact quantity of free hydrochloric acid present in the stomach at the time, and the difficulty, nay, impossibility of such adjustment should be apparent when it is remembered that this quantity (and type) of acid is not known with any degree of certainty. The only practical course would be to select an antacid which, even when present in excess, would maintain this pH, and obviously, the choice would fall on aluminium hydroxide. Magnesium trisilicate, which shows a relatively high pH under ordinary conditions, would also register a somewhat lower pH under ordinary conditions due to the slowness of its neutralising action and would be expected to produce a pH not far from the optimum value.

Subsidiary Effects

It has been pointed out already that although acid neutralisation is the main function of an antacid, some other physiological factors have also to be taken into consideration for its selection. The more important of these are :

1. Effect on the acid-base balance of the blood.
2. Mechanical protection to damaged tissues.
3. Gas formation.
4. Stimulation of secondary acid secretion.
5. Adsorption of toxins.
6. Peptic inhibition.
7. Action on the bowels.

Acid-base balance—The pH of the human blood is delicately balanced between the values 7·33 and 7·51, and the extreme limits compatible with life are 7·0 and 7·8 (Sherman, 1937). This constancy of pH is attained through the agency of buffer systems in which alkali metals constitute the base. When alkali metal compounds, *e.g.*, sodium bicarbonate, are taken as antacids, their absorption from the intestines into the circulation tends to alter the alkali content of the blood and thereby to disturb the acid-base balance. The frequent administration of alkalis, in big doses, is therefore considered undesirable as it might lead to "alkalosis".

Adsorption—Mutch (*loc. cit.*) showed that magnesium trisilicate has a strong adsorbing power for toxins. It should therefore act as an intestinal

detoxicant if taken in sufficient doses so as to pass undecomposed into the intestines. Aluminium hydroxide and possibly magnesium hydroxide also possess adsorbing powers to a greater or less extent.

Mechanical protection—In gastric ulcer, the lesions need protection from the corroding action of acid and pepsin. Bismuth carbonate and also the subnitrate are often used for this purpose, as these have the property of forming an impervious coating on the stomach linings. But these exert no antacid action. A similar protective action is also afforded by colloidal or gelatinous antacids, *e.g.*, cream of magnesia and the hydroxide (Woldman and Polan, 1939), phosphate or silicate of aluminium, which are doubly helpful, as they reduce the acid concentration as well.

Gas formation—Carbon dioxide gas is evolved by all carbonate or bicarbonate antacids on reacting with the acid in the stomach, and such antacids are contra-indicated where gas formation is undesirable.

Secondary acid secretion—When the stomach contents are suddenly neutralised or rendered alkaline by the administration of antacids, a secondary secretion of acid takes place, known as "rebound acidity". According to Opizzi (1944) some substances have a short neutralising effect but produce a secondary increased acidity, *e.g.*, $NaHCO_3$ and MgO; others have the secondary effect without initial neutralisation, *e.g.*, $CaCO_3$, Na_2HPO_4 and Ca_3PO_4 and good neutralisers without much secondary action are $Mg_2Si_3O_8$, $Mg(OH)_2$ and $Al(OH)_3$.

Peptic inhibition—The corroding action of pepsin on the ulcerated parts of the stomach can be controlled by reducing the acidity, but certain antacids, *e.g.*, $CaCO_3$, $Al(OH)_3$ and $Mg_2Si_3O_8$ are believed to possess specific pepsin inhibiting effects (Warren *et al*, 1943). For the same pH, $Al(OH)_3$ exerts a greater inhibiting action than $CaCO_3$. The phenomenon appears to be related to the adsorption of the enzyme on the antacid.

Action on the bowels—Milk or cream of magnesia is well known for its laxative property. Bismuth carbonate, calcium carbonate and aluminium hydroxide on the other hand exert a constipating action.

Some Modern Antacids

The present day trend in the field of antacids is to control the acidity so as to maintain it at the optimum level, at the same time avoiding the undesirable side effects. Buffer systems consisting of alkali salts of weak acids, *e.g.*, sodium acetate, trisodium citrate and disodium phosphate are often used in place of the bicarbonate. Synthetic calcium silicate (Pedersen, 1942) and tricalcium phosphate are also sometimes administered. Magnesium trisilicate and colloidal aluminium hydroxide may be regarded as the most prized antacids of the present time (Shiffrin and Warren, 1942; Wyllie, 1940). The former is now included in both the British and United States pharmacopoeias and the latter finds a place in the U. S. P. XII. The characteristics of magnesium trisilicate from the pharmacopoeial standpoint have recently been discussed by Mukherjee *et al* (1946). Aluminium hydroxide, both in the gel and powder form, has a tendency to lose its acid neutralising power (Johnson and Duncan, 1945) and great care is necessary in choosing the right type of the medicament. Other aluminium salts, *e.g.*, the phosphate, and silicate in the gel form have been suggested as alternatives to the hydroxide, and perhaps the latest in the field is aluminium amino acetate (Krantz *et al*, 1944) which is administered in the dry form. Milk has long been known to have a soothing and beneficial action in hyperacidity and is now often given along with other antacids, *e.g.*, calcium carbonate or aluminium hydroxide (Breuhaus and Eyrly, *loc. cit.*; Rosette and Flexner, 1944). Very recently even aminoacids have been recommended for use as antacids (Devy and Silver, 1943) on account of their amphoteric character.

Conclusion

It is often found that any single antacid fails to satisfy all the requirements of the patient, and combinations of antacids are given to remedy this drawback. Thus, a little quick acting antacid is added to a slow acting one in order to give immediate relief to a suffering patient. Similarly, an antacid having laxative action may have to be added to another having astringent properties. For example, it has been suggested (Rosette and Flexner, 1944) that a combination of 4·0 c.c. of milk of magnesia with 200 c.c. of colloidal aluminium hydroxide prevents the undesirable rise of pH caused by milk of magnesia and the constipating effect of aluminium hydroxide. It is possible to prepare any number of combinations of antacids by varying the ingredients and their proportions, and the number of such preparations in the market is swelling rapidly. Combinations of antacids with a variety of other drugs are also being offered. But a knowledge of the fundamental properties of the antacid substances, chemical as well as physiological, would be the surest guide for making the right choice.

References

Breuhaus, H. C. and Eyrly, J. B.—*Ann. Int. Med.*, **14**:2285, 1941.

Gill, A. M. and Keele, C. A.—*Brit. M. J.*, **2**:194, 1943.

Johnson, E. H. and Duncan, J.—*Pharmacol. J.*, **155**:64, 1945.

Krantz, J. C., Kibbler, D. V. and Bell, F. K.—*J. Pharmacol.*, **82**:247, 1944.

Levy, J. S. and Siler, K. A.—*Am. J. Digest, Dis.*, **10**:48, 1943.

Mukherjee, S., Das Gupta, K. K. and Banerjee, R. P.—*Quart. J. Pharm. & Pharmacol.*, **19**:14, 1946.

Mutch, N.—*Brit. M. J.*, **1**:143, 205 & 254, 1936.

Opizzi, J.—*Semana Méd* (Buenos Aires), **1**:521, 1944.

Pedersen, J. B.—*Danak. Tids. Farm.*, **16**:89, 1942.

Rosette, N. E. and Flexner J.—*Ann. Int. Med.*, **18**:193, 1943.

Rosette, N. E. and Flexner J.—*Ibid.*, **21**:119, 1944.

Schiffrin, M.J. and Warren, A.A.—*Am. J. Digest. Dis.*, **9**:205, 1942.

Sherman, H.C.—Chemistry of Food and Nutrition, 5th Ed., 1937, p. 262.

Starling E.S.—Principles of Human Physiology, 7th Ed., 1936, p. 510.

Warren, I.A., Front, J. and Kirsner, J.B.—*Gastroenterology*, **1**:521, 1943.

Wiggers, C.J.—Physiology in Health and Disease, 1934, p. 767.

Woldman, E.E. and Polan, C.G.—*Am. J. Med. Sci.*, **178**:155, 1939.

Wyllie, D.—*Edinburgh M. J.*, **47**:336, 1940.

BRAIN WAVES

SIBTE ZAIDI, M.B., B.S.,
K. G. Medical College, Lucknow.

Introduction

Pinel, the great alienist of his days, considered stomach to be the primal seat of insanity. Poets and philosophers sang the superiority of the heart over all other viscera of the body. To the heart were attributed all the afflictions of love and hate, of emotion and impulse. It was the guide and the conductor of the human orchestra till Robert Burton, several centuries ago, approached nearer truth and came to regard the brain as the chief organ. Many were the speculations on the location and process of thought in days gone by, and though it may appear ridiculous, scientists are still groping blindly for the answer. Methods of introspection, the Gestalt psychology, psycho-analysis, behaviorism, conditioned-reflexes, have all contributed much of value, but we are still very far from a clear conception of the functioning of the brain. So little, in fact, is known about its functioning that minute anatomy instead of real physiology fills the pages of the standard text-books of the day.

Such a state of intellectual stagnation through dearth of knowledge among neurologists makes any substantial work in this direction of the utmost importance. And such an advance has been achieved in recent years through a study of the electrical changes that take place in the cerebral cortex.

Brain Waves

The brain, the most complex organ of the body, works silently, and, unlike the heart, without mechanical movements. Like the heart, however, it generates electricity, which can be detected, recorded, and even interpreted. This electrical activity produces rhythmical waves of potential variations at characteristic frequencies. These are conveniently termed 'brain waves'. Being first discovered and recorded by Berger, they were earlier referred to as 'Berger waves'. On the other hand all modern references to the subject have been made under the caption of 'electroencephalography'.

Technique of recording.—These cortical potentials of the brain through complicated electrical instrumentation and technique borrowed from radio and television are recorded from the surface of the scalp with no discomfort or inconvenience to the patient.

Electrodes are applied to the scalp at regions under observation and led off through amplifiers consisting of thermionic valves to the oscillograph.

Berger employed needles which he attached to the scalp after local anaesthesia. Marinesco and his associates used, besides the method of Berger, another, in which they applied unpolarizable electrodes to the shaved scalp.

Nature—The graphic record obtained in this manner presents an apparently complicated series of oscillations. But the waves and the patterns that they form are by no means random. Certain wave-lengths and certain definite rhythms strongly dominate the usual records. Voltages are circumscribed within quite definite limits.

As the most constant characteristic of an E. E. G. we come across the frequency of the alpha waves, which is 8-10 per sec.. These waves are of a maximum potential of 0·2 millivolts. This rhythm is remarkably constant in a given individual, maintaining the same level during the entire duration of the recording. In addition, waves of a greater frequency (17-30) per sec.) but a smaller amplitude, which are superimposed on the first, can also be differentiated and are known as beta waves.

The waves are largest when needle electrodes are pushed through the scalp in a region where the skull has been removed, thus strongly suggesting that they arise in the brain. Besides, they are dependent neither on respiration nor on pulsation, and consequently they must be an electrical rhythm of the cerebral cortex.

Prof. Dr. Hans Berger of Jena, who is the inventor of the electroencephalogram, on the basis of his original observations regarded the alpha waves of the E. E. G., popularly called "Berger waves", after his own name, to be due to synchronised rhythmic discharges from neurones mainly in the visual area of the occipital cortex. The waves, as originally observed by him, were present only in the absence of visual activity—appearing normally when the eyes were closed and disappearing as soon as they were opened. The essential condition for the presence of the waves was that the central part of the visual field must be uniform. These waves disappeared by the presence of a pattern.

It was explained that the Berger waves originated from occipital cortex undisturbed by any visual afferent impulses. Any form of visual activity broke up this regular pattern into a complex mosaic of asynchronous discharges and the rhythm was lost.

This view was later supported by Adrian and Mathews who similarly assumed that the alpha waves originated in the occipital cortex only. Dr. Berger however published a further report on his investigations in 'Forschungen und Forlsschritlee' in which he expressed his opinion that the electroencephalogram and its greater oscillations, the alpha waves, develop in man throughout the cerebral cortices and not as Adrian and Mathews continued to maintain, only in the occiptial cortex.

It may be pointed out here that even the earlier reports of Berger mention that alpha waves were obtained on the application of electrodes to the scalp of the man *preferably* to the occipital region. Reports from other workers and Berger himself have however settled the point of discussion beyond dispute.

In the report already referred to, Berger further elaborated his discussion. He rejected his former working hypothesis according to which the alpha waves of the electroencephalogram were considered an

expression of psychophysiological action in the cerebral cortex. He inclined towards the assumption, (based on experiments carried out by Dusser and Barenne and Mac Culloch), that the alpha waves develop in the three lowest cell layers of the human cortex, the so-called corona radiata. He also believed that many of the lesser, briefer oscillations of the electroencephalogram are produced in the uppermost cell-layers of the cortex, the superficial zone. Numerous anatomical, physiological and pathological observations attest to the specially close inter-relation of the superficial zone and psychic activity. Berger sought to establish this region as the place of origin of beta waves of from 11 to 24 angstroms. The relation of beta waves with psychic function has been evidenced convincingly by indicative alterations in the beta waves under a diversity of psychic phenomena.

There is one place where Berger's idea can be said to have been misconceived. He, in another paper read at the International Psychological Congress in Paris in 1937, reported that there existed only a single electroencephalogram for the entire brain. This would imply that the bio-electrical activity is the same in all parts of the cortex.

Prof. A. Baudoin and his co-workers presented a paper in which their study of the question failed to corroborate the observations of Berger. They presented an elaborate discussion based on experiments using multiple electrode-amplifier-oscillographs for different regions. They found, for example, that the activities of precentral and occipital regions were independent even though both the regions are the seats of alpha waves which coincide only occasionally. Homologous regions at the two hemispheres may give rise to tracings which resemble one another, but they were without total concordance in the time of acceleration of alpha waves. The conclusion from these observations is that all cortical nerve areas have their independent electrical activities, but that the latter are more or less coordinated.

We see thus, that the complex and apparently inapprehendable graphic records are no more meaningless tracings of cortical potential variations.

We have not only distinguished certain characteristic regularities in the form of alpha and beta waves, but we have been able to establish their relation to the lower cortical activity (in corona radiata) and higher psychical functioning (in the superficial zone). We have, besides, known that each cortical nerve region has its own independent bioelectrical activity.

We should, however, remember that we have done very little. The elementary classification of waves and their tentative interpretation does not mean more than mere familarity with the graphs. Yet, even with this minimum familiarity with the vastly complex electroencephalogram, we have gone ahead to the application of the elementary knowledge we have with advantage to human problems. The huge amount of subsequent work on this subject has been done mainly keeping this in view. During this work the observations and conclusions just mentioned are automatically confirmed, as indeed the work is based on their preliminary assumption. In fact routine electroencephalographic investigations in a few advanced hospitals are being carried out on a regular basis and are proving useful.

From the brief discussion that follows, of the recent advances in this direction it will be readily understood that the work that has been done by different authors does not throw much light on the nature of these waves, being mere correlation of apparent irregularities in the electroencephalogram with a supposed corresponding clinical condition.

Application of Electroencephalography to Human Problems

The rough idea that we have of the *normal* electroencephalogram in a healthy individual leads us to a study of any apparent irregularity and its interpretation in healthy as well as diseased subjects.

Marinesco and his associates studied the general aspect of this problem. They regarded as anomalies, considerable diminutions and augmentations which occur transiently in the course of recording. On the other hand, the amplitude of the waves varies considerably in the course of recording. They found that in some pathological cases the anomalies of the electroencephalogram consisted specially in modification of the amplitude (epilepsy and tetany) or of the amplitude and of frequency (aphasia, cerebral tumours) and so on. The pathological cases with modifications of the frequency but without changes in the amplitude are extremely rare; nevertheless there are exceptions. In some of the reported cases of aphasia, for example, frequency alone was diminished, likewise in dementia. In two cases of cerebral tumours an augmentation of frequency without modification of amplitude was encountered.

The general aspect of these irregularities having been thus worked out by Marinesco and his associates, other workers in the field were not wanting to contribute their toil in the respective diseases peculiar to the brain. Major contributions were accordingly made in the field of epilepsy and intracranial tumours and lesions.

I. *Epilepsy*—The pioneers in the field of epilepsy are Gibbs and Lennox of Boston. They electroencephalographed more than 400 patients and discovered several new facts about epilepsy, leading to improved diagnosis of epilepsy and an increased understanding of the nature of epilepsy and its genetic characteristics. An epileptic seizure, whether a generalised or a brief lapse of consciousness, is almost always accompanied by dramatic changes in the electroencephalogram. The convulsive seizure is associated with the appearance of sharp fast waves of moderate to high voltage in rapid sequence with, or without, the presence of slow large voltage flat-topped waves (often called delta waves) in addition. It is most significant that these successive electric discharges, obviously the picture of overactivity, usually begin many seconds before the muscular movements or loss of consciousness. Besides, the epileptic patient between seizures frequently

shows in the electroencephalogram 'spikes' or runs of fast waves resembling the preliminary outbursts that precede his convulsion but without signs or symptoms associated with them. The patient is unaware of them but they are diagnostic of a susceptibility to seizure, and in a patient subject to seizures an increase in number and intensity of larval outbursts may give warning of an approaching convulsion hours or even days before. The abnormal rhythms are thus clearly the *cause* of seizure and certainly not the effect. The more fundamental basis of disorder, however, is not the abnormal rhythm but rather a defective control of rhythm. Gibbs and Lennox, therefore, conclude confidently that epilepsy is the expression of improper functioning of the rhythm-regulating mechanism of the brain. In short, the pathological physiology of epilepsy is a paroxysmal cerebral dysrhythmia. Golla, Graham and Walter, who are the other workers in the field, however, adopt a more cautious attitude towards the problem. They considered that 'no definite pronouncement was possible as to the significance of the delta-wave foci in epilepsy.' Their observations however, corroborate those of Gibbs and Lennox, and therefore do not leave much doubt as to the validity of their conclusion.

Both groups of workers are in accordance regarding the fact that the form of these abnormal rhythms is distinctive for the *three main .clinical .types of seizures*—petit mal, grand mal, and the psychomotor type.

The loss of consciousness for only a second or more with or without minor muscle twitches of the face and the eye, known as the petit mal, shows large slow waves at a frequency of almost exactly three a second with one or several sharp 'spikes' alternating, this being the most characteristic pattern of petit mal.

A grand mal or a major convulsion is preceded by an outburst of fast waves with a frequency of 10 to 30 per second. With the onset of the seizure the voltage rises. Between the fits slow waves of large voltage—the delta waves—appear. Abnormal rhythm preceding these and even other types, commonly appear first in the frontal area, but may even arise first in the parietal or occipital areas.

It should be emphasised that although typical patterns may be described as corresponding to grand mal and petit mal respectively, it is seldom so clear and simple. Most actual seizures are composite and show a mixture of grand mal and petit mal patterns.

The third variety of seizures, called the psychomotor type, in which the patient does not completely lose control of himself or become unconscious, has again its own characteristic rhythm. It is primarily a slow rhythm, about six a second, and the waves are often unsymmetrical and monophasic. Patients whose fits are symptomatic or hysterical gave normal records.

Many varieties of electrical patterns and many gradations of odd and unusual behaviour are seen, and the clear diagnostic electric patterns and definite clinical manifestations merge gradually into what are called 'generally dysrhythmic electroencephalogram and behaviour problem individuals.'

There is a significant group of men and women who never have had seizures but show the same types of dysrhythmia as described. Irregularity of electric activity in them is certainly not epilepsy but it reveals the soil in which the epilepsy grows. It is suggested that it is primarily those with the dysrhythmic electroencephalograms who develop secondary or symptomatic epilepsy following an injury to the brain (Lennox). Equally important is the fact that cerebral dysrhythmia is a hereditary characteristic that is almost always found in the epileptic himself and among his relatives. Here apparently is the hereditary element in epilepsy—the potentiality for seizures—that is far more common and widespread in the population than the incidence of actual seizures (Gibbs).

In these works on epilepsy we not only see the dreams and prophesies of Berger coming true but even much more than that. Not only the *different clinical types can be diagnosed correctly,* but *seizures predicted, hysterical and symptomatic fits differentiated,* and the *susceptibles picked* out from a pack of apparently healthy people.

Treatment of Epilepsy—And finally, electroencephalography may be useful in the treatment of epilepsy.

In one instance, reported by Gibbs and Lennox, where the abnormal rhythms were confined to the frontal area, the interior portions of both frontal lobes were removed, with subsequent virtual disappearance of abnormal rhythms and great improvement in seizures. It is only a solitary instance of surgical interference with the help of electroencephalogram. On the medical side it is bound to be a greater importance. Not that by itself it is in any way a cure, but it may be used to determine what drugs and what dosages are best suited to the need of a particular case. The number and prominence of larval subliminal episodes are greatly reduced in most cases by appropriate medication. But, instead of waiting for weeks or months to determine the effectiveness of different combination or altered dosages, we may now gain an indication in a few hours, or at the most a few days, of the effectiveness of the medication by simply observing the degree of stabilisation of the electroencephalogram.

We owe, for example, to electroencephalography alone the important discovery announced by Gibbs and Lennox in 1939 that carbon dioxide will influence the epileptic seizures. Petit rhythm and a seizure may be precipitated by a short period of over-ventilation by which process carbon dioxide is pumped out, and conversely may dramatically disappear while the patient is breathing air containing 3-7 per cent of carbon dioxide.

We see now, although this method of investigation in diseases is only seven years old it has already contributed enormously to the understanding of the pathological physiology of epilepsy. It warrants the hope that methods of treatment can be improved by objectively observable means and portends a greater degree of individualized effective therapy.

II. *Intracranial Lesions*—LOCALISATION OF TUMOURS.

The next of the important practical applications of electro-encephalography is the detection and localisation of intracranial lesions. The principle, first applied by Walter, is extremely simple. Cortical potentials of different regions are recorded by the multichannel recorder which writes simultaneously the electroencephalogram of three to six regions.

A tumour or a haematoma does not generate abnormal electrical waves, but if it compresses the neighbouring brain tissue and produces through oedema, partial anoxia or some other condition then a physiological depression appears which gives rise to slow, high voltage electrical waves. Appearance of such waves, therefore, points to a lesion. The region from which it appears points to its localization. Superficial cortical lesions cause the greatest change and, being confined to a relatively restricted area within an inch or so of the electrode, are easily detectable. Deep-seated lesions are evidently less easy to localize. Practical success is evidenced by the results of electroencephalograms of patients taken by various enthusiasts. Dr. R. S. Schwab followed up 417 electroencephalographic localizations made at the Massachusetts general hospital. In 115 cases the localization had been clear and definite, and verification by operation or on post-mortem examination exhibited correct localisation within the area of surgical incision in 84·5 per cent of the cases. In 89 cases where the electroencephalogram gave doubtful evidence and the best guess possible was made at the surgeon's request, accuracy was only 43 per cent. It is important to note that most of these cases showed abnormality in the posterior fossa. Such groups particularly when they caused increased intracranial pressure may be very deceptive for the electroencephalogram. In 213 cases no evidence of focal lesion was detected by the electroencephalogram. Later, 9 per cent showed a focus on necropsy or in the operation theatre, but 91 per cent never came under the surgeon's knife, though the present hospital diagnosis supports the electroencephalographic report. This remarkable degree of success of Schwab is in accordance with the earlier findings of Williams and Gibbs. They worked on 105 cases in which intracranial lesions were suspected and found a close correlation between the actual position of the lesion and that predicted by the electroencephalogram. Actually 35 out of 50 showed actual lesions at the operation table or on necropsy. In another 15 cases clinical evidence was strong and was supported by provious explorations with the help of x-rays and visible changes like skull defect, scalp wound, visible mass, etc. In 41 cases, in which no abnormality was predicted by the electroencephalogram, subsequent clinical examinations too gave negative results. The remaining 14 cases could not well be judged through lack of data.

Schwab seeks to explain the few discrepancies by the following reasons:—

(*a*) Failure to use a sufficient number of electrodes.

(*b*) Bilateral disturbance caused by deep lesions near midline.

(*c*) Counter-coup pressure effects produced by large flat lesions outside the cortex—*e.g.*, subdural haematomata.

Apparently the method has great practical value as a *diagnostic procedure in routine neurological practice*, but we must not be lifted off solid ground through amateur enthusiasm. The electroencephalogram by itself alone is in reality as sure and accurate as roentgenography or neurologic examination, taken alone. It is only a combination, rather a concordance, of any of these 2 that errors in diagnosis could be made negligible. Moreover, the electroencephalogram tells hardly any thing of the nature of the lesion, for what we see is only the reaction of the neighbouring tissues to the mechanical effect of the lesion.

OTHER BRAIN LESIONS: INTRACRANIAL HAEMORRHAGE—As we have seen, electroencephalography has been very useful in the detection of various intracranial lesions, yet it has not been used to any extent in the investigation of cases of head injury. Only a few cases are on record concerning the value of electroencephalogram in cases particularly when intracranial hæmorrhage has occurred. Prof. Rendle Short and Miss Dunster in 1940 published a paper on middle meningeal hæmorrhage in the case of a patient aged 42 upon whom an operation had been performed. Balado, Romero and Noiseus in 1939 gave a paper on electroencephalogram in the case of an Italian aged 41 suffering from chronic subdural hæmatoma. Jasper, Kershman and Elirdge in 1940 noted some examples of intradural hæmorrhage, both extra- and intra-cerebral. The electroencephalographic findings in these cases constitute cumulative evidence of electroencephalography as an aid to the detection and location of traumatic intracranial hæmorrhage.

OTHER ORGANIC DISEASES—In other organic diseases of the brain and in mental disorders the usefulness of the electroencephalogram is still limited. We usually observe only slight changes in the recorded waves, and then too repeated records have to be made. In the cases in which 'slow' alphas, of about 7½ per second, are noted, we may take it for granted that they indicate pathological changes associated with an impairment of cortical function. Unfortunately, investigations done are few and of a limited nature, but we can confidently assert from what is already known that the scope of the electroencephalogram in the diagnosis of these disorders will be greatly increased in the future.

Carbohydrate Metabolism—Hoagland and his associates studid 6 schizophrenics receving insulin treatment, and made 35 records. They found that electrical waves of the brain after large doses of insulin showed a definite slowing in frequency of alpha waves. This, with a time lag of about ½ hour, ran parallel with the *decline* blood sugar curve. Sugar injection during coma restored the frequency along a smooth curve. Along with other evidence we hold that alpha frequencies are directly proportional to the rate of carbohydrate metabolism of the cortical

cells producing the rhythm. This discovery has a possible potential application to disorders of carbohydrate metabolism. If the alpha waves are directly proportional to the rate of carbohydrate metabolism we should expect to use electroencephalographic index during insulin administration.

Brain Waves and Pilots—By far the most thrilling development of the application of electroencephalography to human problems has its use in routine examination of student-pilots.

Its importance in the diagnosis of petit mal, which disease is characterised by loss of consciousness for only a second or more with or without minor muscular twitches in the face and the eye, has already been stressed. The momentary blackouts and losses of memory which are connected with the undiscovered form of epilepsy are of utmost importance for fliers whose attention must never lessen even for one moment. The importance of electroencephalographic investigations to weed out such minor cases which are apt to be overlooked otherwise becomes apparent.

Besides, the susceptible epileptics which do not show any symptom whatsoever may at any time become epileptic with possibly disastrous results. And there is no possible method of diagnosing these except with the help of the electroencephalogram.

It is with these considerations that, under the direction of Major G. E. Hall and J. E. Goodwin, Canada has established a clinical investigation unit of the Royal Canadian Air Force. The United States Navy was so impressed with the results that it has established its own brain-wave clinic at the Naval Training Station at Pensacola, Florida. Hallowell Davis and Alexander Forbes of Harvard Medical School, and Hudson Hoagland of Clark University examined the brain waves of some hundred student pilots there.

At the Boston City Hospital, under the direction of F. A. Gibbs, the Work Projects Administration is preparing standards of normal to be used in classifying student fliers. Of the two thousands students so far examined about one per cent turned out to be marked epileptics.

The brain wave analysis therefore may be of tremendous help in the air service arm.

Suummary of the Work Done

Since 1924 when Berger first started working on the subject till the appearance of the latest reports in the journals, the progress has been two-fold.

One is the specific investigation of the *nature* of the encephalogram and another is its *application* to human problems.

Regarding the *nature* we have learnt to distinguish the alpha and the beta waves and attribute seats of origin to the corona radiata and superficial zone respectively. We have besides, discovered that each cortical nerve region has its own independent bioelectrical activity.

In the field of *application* of electroencephalogram we have learnt to correctly diagnose the types of epilepsy, particularly the petit mal. We can predict the seizures, differentiate the hysterical and symptomatic from the genuine and weed out the susceptibles from a group of apparently healthy people.

We are now approaching a future method of treatment of epilepsy by objective observation of reaction, nearing a greater degree of individualized effective therapy.

We have evolved a diagnostic procedure for localization of tumours, now on the verge of being used as a routine measure in hospitals.

We have also found a direct proportion between the alpha waves and the carbohydrate metabolism.

Last but by far the important development has been the electroencephalographic method of weeding out epileptics from the student pilots, being used extensively in United States and Canada.

The Future of/in Electroencephalography

Electroencephalography is the most direct objective indicator of cortical activity now available. An electroencephalogram is a true record of what the most complex organ in human body is silently doing. The significance of the correct interpretation of this vastly complex record of cortical potential variations should therefore be fully understood. Mere arbitrary classification of the waves into alpha and beta on primary consideration of frequency does not mean more than a preliminary acquaintance with the meaningful language of electroencephalography. Our present knowledge about the subject is equivalent to recognition of a few letters. We have yet to learn to spell the words—correctly, understand their meaning, corelate them into sentences and thus master the great language.

We do not undervalue the extensive work done on the subject. We maintain, however, that the medical world has been too jubilant over the discovery of a direct method of investigating the crude lesions and maladies of brain. The excitement about the introduction of this method has been such that the most important issue has been side-tracked. That is the investigation *into* the nature of electroencephalogram. The medical world has been enthusiastic to apply the little they know about the "great method", but not, as yet, to human problems. The utilitarian aspect of the subject does no doubt equally deserve our attention, but not all of it.

In our opinion special investigations should be carried to investigate fully and interpret completely the electroencephalogram, and relevant work and literature should be carefully corelated to that end.

A detailed study of the encephalograms of babies will certainly give us the correct knowledge of the basic waves originating in the lower cortex. It has been supposed that alpha waves originating in the lower cortex and that the beta waves are more or less

related to the psychic cortex. It has been further found that an increased activity of beta waves is accompanied by a diminution of alpha waves. We know that higher psychic centres have an inhibitory control over the lower centres. If the beta waves show a similar control the parallelism should lead us to conclude that waves with greater frequencies belong to the higher psychic centres, those with the slower ones to the lower. The existence of faster beta waves should therefore mean more developed higher psychical centres.

The electroencephalograms of the babies should decide the issue. If they demonstrate a preponderance of slow alpha waves this hypothesis should be taken as correct, as the higher psychical areas develop later.

Besides working with the electroencephalogram of the babies we may be able to note the electroencephalographic reaction to the external stimuli. The electroencephalogram of a new born baby may be regarded as a 'pure electroencephalogram'. We may be able to clearly distinguish any superimposed wave on the original characteristic as indicative of an auditory-word memory centre activity. This is only an example. What is meant, in short, is that we may start with a pure basic electroencephalogram of a new born baby and study it as it grows correlating its mental acquirements by resultant electroencephalographic changes if any.

Through large scale work we believe it would be possible to correlate many mental conditions with characteristic encephalographic records.

During investigations of electroencephalograms of the student pilots in America, it may be recalled, an effort was made to pick out from their brain-wave records men who will make the best pilots. Although conclusions are not yet forthcoming the reports are that evidence is mounting that men with persistent alpha waves in the frontal region of the brain do not make good pilots. We see thus a correlation of characteristic electroencephalographic complex a definite mental capability, say the capability of continuous concentration. If therefore we could recognize waves corresponding with and characteristic of capability of concentration we could similarly correlate other wave-complexes with their respective psychic counterpart, memory, genius and stability of character etc.

This at once opens up the great possibility of a direct objective study of personality components. By an extensive investigation into them we could be able to compose a dictionary of personality-components—a breath-taking advance in Psychology! And yet what could be more reasonable than correlate the true records of cortical activity with their psychic counterpart. If the behaviour of an individual is the end result of cortical activity, which it undoubtedly is, we are bound to find the counterpart of every cortical activity in a properly recorded electroencephlogram.

The electroencephalogram should therefore be a basis of experimental psychology.

The electroencephalogram of each individual has its own style just as one has his own style of handwriting. It is reported that it changes little with age once it has reached adulthood. In some persons, reports a recent article, the voltage is a little higher, in some the alpha rhythm a little faster or slower or little less regular and in others there is a little less of alpha activity and more of smaller faster words. "These types of electroencephalorgaphic patterns, therefore, apparently represent constitutional differences and there is an increasing body of evidence that certain aspects of habitual behaviour or 'personality' may correlate with extremes of pattern". The workers on epilepsy have reported that many varieties of electrical pattern and many gradations of odd and unusual behaviour are seen, and the clear diagnostic electrical patterns and definite clinical manifestations of clear-cut types merge gradually into what are called "generally dysrhythmic electroencephalograms" and "behaviour problem" individuals. A high incidence of dysrhythmic electroencephalogram in problem children has also been reported.

A further study on this problem should, therefore, be justly demanded and we will not be surprised if an application of electroencephalogram to criminal investigation and reformatory schools of the juvenile criminals is forthcoming as a result.

An application of this to other aspects of psychology could also be imagined. We could explain likes and dislikes of individuals. We could seek to explain the liking of an individual for another on the basis of sympathetically vibrating electroencephalograms. It is not a fantastic idea, as identical twins always have closely similar patterns of the same type. Love, if it has any basis besides sex may happen to depend a great deal on a similarity of brain waves. The electroencephalograms of two individuals who have a strong liking for each other may not show much similarity in adulthood. We may suggest, however, that the similarity may be in the 'basic' waves of early childhood and not in the later superimpositions which are a result of environments.

With a few facts here and there in accordance with our views on the future of/in electroencephalography, we may say with some degree of confidence that electroencephalography has in store for us great developments in experimental psychology and treatment of diseases of the brain.

References

Adrian, E. D., and Mathews, B. H. C.—*Lancet*, **2**:311, 1934. *Idem*—*Ibid.*, **1**: 1935.

Burlimgame, C.—*J.A.M.A.*, **113**:377, 1939.

Davis, H.—*J.A.M.A.*, **117**:983, 1941.

Gibbs, F. A., Gibbs, E. L. and Lennox, W. G.—*Brain*, **60**: 377, 1937.

Howell, W. H.—A Text Book of Physiology, 1941.

Lennox, W. G., Gibbs, E. L. and Gibbs, F. A.—*J.A.M.A.*, **113**:1002, 1939.

Roger, L.—*Brit. M. J.*, **1**:511, 1941.

Short, A. Rendle and Dunster, M.—*Brit. M. J.*, **1**:884, 1940.

Walter, W. G.—*Lancet*, **2**:305, 1936.

Wright, W.—Applied Physiology, 1941.

CASE NOTE

PLASMODIUM OVALE INFECTION IN U. P.

An Interesting Case of Malaria

N. TYAGI, CAPT. I.A.M.C.,
Officer I/C. Station Laboratory.

The case is by no means unique, but in view of the very mild nature of the attack, spontaneous clinical and parasitological cure, oval shape and enlarged size of the infected erythrocytes, preponderance of Schuffner's dots and the presence of various unusual and paradoxical forms of parasite, it certainly becomes a really interesting case.

CASE REPORT

H. A. K., a Mohammedan male, aged 24, was admitted complaining of fever with rigor the previous night.

He had normal temperature for two days in the hospital. On the third day afternoon, his temperature suddenly shot up to 103° F. with rigor. Blood smears were found positive for malaria, but antimalarial treatment was not instituted as some uncommon forms were seen in the smears. No previous history of malaria was available. Next day the smears were re-examined, the abnormal forms were confirmed and a supply of two hourly blood smears requested.

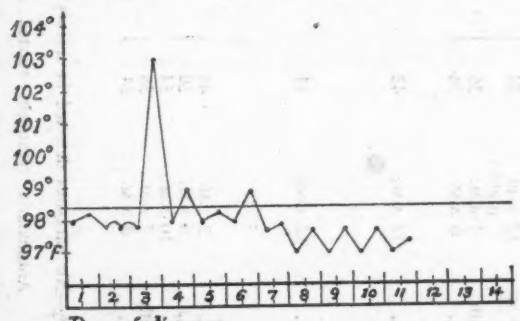
It would be seen from the temperature chart that the patient ran a very mild course of the disease and that the clinical recovery occurred long before the antimalaria drugs were administered on the 11th day.

The figures show camera-lucida drawings of some of the parasites seen in thin blood smears, which were stained by Leishman's stain for five minutes. Attempts have been made to make them as representative as possible. The table gives the description of the average characteristics of the parasites seen.

COMMENTS

The following special characters of the case may be noted.

(i) *Temperature chart*—The chart shows that the patient ran a very mild course of fever and that the clinical and parasitological recovery occurred some days before the anti-malaria treatment was instituted on the eleventh day.



TEMPERATURE CHART OF THE REPORTED CASE

A mild attack with spontaneous recovery is said to be the characteristic of *P. ovale*, but it is by no means uncommon in relapse cases of *P. vivax* and *P. malaria*. J. G. Thomson, in *Trans. Roy. Soc. Trop. Med. & Hyg.* Vol XXVI, pp. 483-514, has shown that after spontaneous recovery from benign tertian malaria an immunity to superinfection develops, which is, however, specific in character. Although an exact proof of the presence of immune bodies in the system is still lacking, there is no doubt that the so-called 'tolerance', 'premunition' or 'relative immunity' does develop as the result of previous infection—but in the case, under review, there was no history of previous attacks of malaria. In addition, heredity or racial immunity may play a part too; but that too does not seem to be applicable in this case.

(ii) *Rigor was in the evenings*—Fairley, Muhlens and others (Manson's Tropical Diseases, 1945, pp. 843) state that the paroxysms of fever due to *P. ovale* infection come on in the evening or at night. This discrimination, however, is rather misleading, since it has been observed that certain typical cases of *P. vivax*, *P. malaria* or/and of *P. falciparum* infection are associated with attacks beginning in the night or early in the afternoon.

(iii) *A large number of the infected erythrocytes were oval, slightly enlarged and showed Schuffner's dots*—In *P. ovale* cases the infected cells are said to be oval, but generally not much enlarged; while in *P. vivax* infection the reverse is the case. Schuffner's dots seen in both the types of infection were also found in the case—these could not be confused with Zieman's stippling, which are characteristic of *P. malaria* infection and take much longer time to be stained by the Leishman stain. Diagrams show that a large proportion of the infected cells are oval, though the margins are not typically fimbriated.

(iv) *Some atypical and confusing forms of parasites seen.**

(*a*) *Band forms*—(*specimen* 43 *vide* Plate). In *P. ovale*, although the parasites more nearly resemble *P. malaria*, band and ribbon forms so characteristic of the latter, are generally held to be absent. Manson Bahr in his book on Tropical Diseases, states that in *P. ovale* cases parasites give an appearance which in all the stages of its growth resembles *P. malaria* but differ from it by the absence of band forms. Band like forms are NOT seen in *P. vivax* or/and *P. falciparum* infection.

(*b*) *Tennue forms*—(specimens 29 & 35 *vide* Plate) are suggestive of *P. tennue* infection. Stephen described a P. tennue form of malaria, when peculiar species were seen by him in a single blood film sent him from a case

* Out of 58 specimens drawn a selection was made and only 12 essential and representative ones reproduced (see Plate).

TABLE—SHOWING THE COMMON CHARACTERISTSCS OF THE PARASITES

Day of Disease	Smear taken at	Hours after first rigor in hospital	Specimen number	Size & shape of infected erythrocytes	Pigment	Characters of the trophozoites	Schizonts	Gametocytes	No. of parasites per field
3rd	4 P.M.	0	1-10	Slightly enlarged and generally oval. Schuffners' dots well marked.	Nil	Large vacuolated and solid forms occupying a major portion of the cells. Chromatin well marked. Accole forms not seen.	Nil	Nil	1-2
4th	2 P.M.	22	11-18	Slightly enlarged some oval, and paler in colour. Schuffner's dots not marked.	Coarse brown in some.	Tendency to assume tennue forms. Cytoplasm detached, chromatin well marked, and in some even divided.	Nil	Nil	1 or less
"	4 P.M.	24	19-28	Enlarged. Schuffner's dots present.	Well marked, some brownish black.	Band forms frequently seen. Chromatin marked.	No typical ones seen.	Nil	1 per 3-4
"	6 P.M.	26	29-36	Less enlarged and mostly oval. Schuffner's dots scarce, and paler in colour.	Scarce.	Tendency to tennue forms, chromatin well marked.	Nil	Nil	1 or less per 3
"	8 P.M.	28							
	10 P.M.	30							
4-5th	12 Midnight	32	37-42	Slightly enlarged, many oval, Schuffner's dots variable.	Coarse, brown.	Band, solid forms and some wide rings seen. Detached masses of cytoplasm frequently seen. Chromatin prominent and divided in some.	No typical ones detected.	Doubtful. None typical seen.	1 per 3-4
5th	4 A.M.	36							
"	6 A.M.	38							
"	10 A.M.	42	43-51	Somewhat enlarged, some oval. Schuffner's dots marked in most.	Coarse brown, tendency to aggregation.	Some band forms. Division of chromatin frequently seen.	Earlier forms seen. Merozoites six or less.	Doubtful and scarce.	1 per 5-6
"	12 noon	44	52-58	Enlarged, some oval. Schuffner's dots fewer present.	Mostly aggregated, dark brown.	Division of chromatin, with masses of cytoplasm.	Present. None with more than six merozoites.	Very scarce.	Hardly 1 per 10
"	2 P.M.	46							
"	6 P.M.	50							
"	10 P.M.	54							
6th	2 A.M.	58	..	The characteristics of the parasites were similar to those described above (Specimens 52-58) but their number per field gradually diminished so much so that in certain films not more than two or three were detected after prolonged and thorough search.					
"	8 A.M.	64							

N. B.—No parasites detected in smears taken on the 8th day of disease at 12 A.M. and 4 P.M., on the 9th day at 2 P.M. and 6 P.M. and on the 10th day at 3 P.M. and 7 P.M.

Antimalaria treatment started on the 11th day of disease at 8 A.M.

in India in 1914. Sinton was inclined to support his contention that it was a separate species; while Belfour and Wenyon considered tennue forms to be not uncommon in *P. falciparum* infection. On the other hand, Chamars and Archbald described a tennue phase of *P. vivax*, stating that altered forms of parasites are not uncommon in cases with spontaneous recovery as a result of the development of some complex protective mechanism.

In the case under review, there appears to be a tendency to spontaneous recovery, and, therefore, somewhat small forms of parasites may well have been brought about by the degenerative process due to the action of body protective mechanism—this sounds highly theoretical in the absence of previous attacks of malaria.

(*c*) *Schizonts with more than six merozoites not seen*—This is characteristic of *P. malaria*, and is also a common feature of *P. ovale*, which resembles the former in many ways.

It is, however, true that often in typical *P. vivax* cases most of the schizonts seen in the blood films do not show more than 6-8 merozoites for the simple reason that these are really early schizonts—typical and mature ones being rarer to see. In this case, never-the-less, not even one was seen to contain more than six merozoites despite prolonged and very careful search of the blood films, especially that taken 44 hours after the rigor.

Discussion

It would appear that the case cannot be one of *P. falciparum* or that of *P. tennue*, since in these infections the largest forms of the parasites seen in the peripheral blood are held not to exceed half the diameter of the infected erythrocyte. This fact is not borne out by the blood smears of the case. Besides, the presence of enlarged r.b.c.s. and that of the marked Schuffner's dots are also against these infections.

Band forms suggest *P. malaria* infection, but the enlargement of erythrocytes and the presence of Schuffner's dots rule that out. These dots could not possibly be Zieman's stippling as the Romanowsky stain was not left on the slide for more than five minutes.

The possibility of its being a mixed infection of *P. vivax* and *P. malaria* are rather remote for the reasons that (*a*) such an infection is very rare and (*b*) if it were a fresh double infection there should have been many more paroxysms of fever; and if it were a relapse it looks highly improbable that the two infections would appear and disappear simultaneously.

It, therefore, now remains a case of benign malaria either an infection of *P. vivax* or that of *P. ovale*.

Enlargement of erythrocytes, presence of Schuffner's dots and the presence of many stages of the parasite in the same blood smear are pathognomonic of *P. vivax;* but the presence of band forms, and the fact that none of the schizonts, in any of the smears taken at different times, shewed more than 6 (six) merzoites are paradoxical.

The presence of oval infected erythrocytes, dark brown pigment as against the pale brown of *P. vivax*, early division of chromatin, evening rise of temperature and the spontaneous cure (both clinical and parasitological) are the points which can not be overlooked, and the diagnosis of malaria *P. ovale* should not be lightly brushed aside on the flimsy basis that such an infection has not previously been reported in the station.

Summary

A case of malaria *P. ovale* is described.

Camera lucida pictures of the infected erythrocytes have been reproduced. Attempts have been made to draw the diagrams of the specimens as actual as possible in colour and size as seen under 1/12" oil immersion lens.

Unusual findings have been discussed, in relation to various possible diagnoses.

Conclusion

From the discussion it is apparant that the balance of evidence is strongly in favour of the case being one of *P. ovale* infection, although by no means a typical one.

It is very much regretted that the slides could not be produced before the expects now. This case was noted some years back and because of the peculiarity of the cases the slides were sent overseas with the article. The personal opinion of experts differed but the consensus of opinion seemed to favour the diagnosis given herein. It was to the author's greatest regret that slides were lost in transit during the war conditions. He is, however, extremely grateful to the authority for having conceded to publish it and he must naturally take the responsibility for the correctness of the statements.

JOURNAL OF THE
INDIAN MEDICAL ASSOCIATION

CALCUTTA, OCTOBER, 1947

THE PROBLEM OF HUMAN STERILITY

By far the largest majority of cases in gynæcological practice is centered round conception and childbirth. Some of them want babies and cannot have them. Some have had enough and want no more, while others seek relief from conditions which are the outcome of childbirth. From the records of three large hospitals in India it appears that a little over 10 per cent of hospital admissions are for the treatment of sterility. But when is a woman to be considered sterile? Matthew Duncan put it to three years after marriage. But modern civilisation and social consciousness of young men and women often complicates this definition. The question of voluntary contraception comes in. Statistics from maternity hospitals show that the largest number of primiparous confinements take place within three years of marriage. But hospitals receive patients from all classes. The figures obtained from four private nursing homes in one of the largest cities in India however indicate that no less than 70 per cent of primiparous confinements take place five years or more after marriage. It would thus be better to consider each case of sterility on its own merit considering among other things the personal history of the couple.

Only about twenty years ago investigation of a case of sterility consisted in the discovery of a congenital abnormality, tented vagina, pinhole os, cochleate or fibroid uterus, tubo-ovarian mass or some other gross abnormality. If these were absent, and the fallopian tubes were patent, dilatation and currettage and "hard prayer" were all that was advised as treatment. In the times that have gone by, we have known more about the physiology of conception, though this knowledge has been yet far from complete. Indeed, the process is so complex that one should wonder as Bourne[1] suggests, at the frequency of successful conception rather than at its occasional failure.

When obvious pathological lesions are present a case seldom presents an obstacle. But when it is not so, the condition of so called functional sterility, frequently defies elaborate investigations. This holds good even in the case of the male partner. Sperm cell count has been known to be important for a long time. The recent interesting experiment of Chang[2] shows fairly conclusively the effect of sperm cell concentration on the fertilising capacity of the semen. This author inseminated 20 doe rabbits with known number of spermatozoa in different dilution, and studied the number of cleaved ova obtained. He observed that 17 to 42 per cent, 0 to 28 per cent and 0 to 6 per cent of the ova were cleaved when a similar number of spermatozoa (30,000-44,000) were suspended in 0·1, 0·4, and 1 c.c. of saline. He also observed that the maximum of only 19 per cent cleaved ova were obtained when the number of spermatozoa were doubled (80,000) but suspended in 1 c.c. of saline. It thus appears that what is important is not merely the number of sperm cells in the seminal fluid, but the concentration of it. Nevertheless, mere number and concentration are not the only things that matter. Dead sperms do not fertilise, nor do the abnormally formed ones. Douglas[3] in an investigation found that when abnormal forms made up 25 per cent of the total, sterility was the usual rule. Viability of the spermatozoa is another important factor. The application of this in another form is in Huhner's test which is quite widely employed in most sterility clinics. Viability and motility have however been shown in recent years to depend on the normal metabolism of the semen. Mann[4] demonstrated that for metabolism of the spermatozoa in anaerobic conditions, as happens normally after insemination, fructose must be an essential constituent of the semen (glucose can also be similarly utilised but fructose is better). Fructose is added to the seminal fluid by the vesicles and the prostate. This enters into combination with adenosine triphosphate present in the sperm cells and passes through a chain of reactions to lactic acid. Ivanof, Kassafina and Fomenko[5] also showed that under these conditions adenosine triphosphate decreases, and with it also the motility of the sperm cells, which is restored on the addition of glucose. The first two authors (*loc. cit.*) also showed that the activity of the sperm cells could be increased markedly, adding prostatic secretion to the spermatozoa. These recent investigations demonstrate that the functional activity of the spermatozoa depend not merely on the number and formation, but also on the function of what have been known heretofore as accessory organs of generation. Thus investigation of the husband also includes a careful inquiry into the physiological activity of the prostate and seminal vesicles. The normal content of fructose in the semen has not yet been definitely known, much less how it can be increased. The same holds good for the adenosine triphosphate content of the sperms. But when these are known one more avenue for our knowledge in the subject will be opened.

Recent years have also told us about another important role played by the sperms in the physiology of fertilisation. This is the dispersal of corona radiata cells by the enzyme hyaluroniease normally present in the spermatozoa. This enzyme causes the liquefaction of the gel which cements together the cells surrounding the ovary, thereby bringing the spermatozoa in close contact with the membrane of the ovum itself.

[1] Recent Advances in Obstetrics and Gynaecology, 1939.
[2] *Science*, **104**:361, 1946.
[3] *Urol. Cut. Rev.*—**1**:529, 1946.
[4] *Biochem. J.*, **40**:481, 1946.
[5] *Nature*—**158**:624, 1946.
[6] *Am. J. Med.*, **1**:491, 1946.

Kurzok, Leonard and Conard[6], who demonstrated this property of the semen also reported six cases of sterility where application of hyaluroniease to the cervix produced conception. The evidences are certainly not conclusive, but undoubtedly opens a greater vista. Leonard, Perlman and Kurzok[7] also devised a means of estimating, the hyaluroniease content of the semen which is worthy of trial in every equipped laboratory in sterility clinics. Kurzok and others (*loc. cit.*) found that the enzyme content may have a relationship with the sperm count of the semen, 50 million being about the critical point. It has of course been known for a long time that below this level the fertility index in men is low.

Recent years have shown that functional disorders in the female with regard to sterility are principally centered round the behaviour of the ovary and cervix. Ovulation is the primary essential to fertilisation. Menstruation is no longer a certain sequela of ovulation. Anovular menstruation is no more a hypothetical entity. Anovulatory cycles may be found even in normal individuals. Levan and Szanto[8] found the incidence of anovulatory cycles as 8·7 per cent. Approximately about 9 per cent of women have anovulatory cycles while among sterile subjects the incidence increases to about 30 per cent (Bourne, *loc. cit.*).

The estimation of ovulation has then in present years become a subject of considerable magnitude. The simplest means is undoubtedly endometrial biopsy and discovery of secretory change. For all practical purposes this is a simple and reliable method. Samuel's[7] spectroreductometric method demands skill and experience. Determination of walking temperature curves is simple and costs nothing. An intelligent patient can willingly co-operate to keep this chart. We have found this a reliable index of ovulation as verified by endometrial biopsy. The time of ovulation on a W.T. chart should be read at the lowest point of the ebb.

Determination of mere presence or absence of ovulation is naturally not enough. Ovulation taking place within two days of menstruation produces the same effect as anovulation, as fertilisation must occur at least 48 hours before menstruation for embedding of the zygote to take place. History of coitus in relation to the time of ovulation is another important investigation, a point which is not unoften neglected. Fertilising capacity of the spermatozoa does not probably last for more than two days after insemination. The viability of the ovum also is probably not more than 24 hours after ovulation and certainly not more than 48 hours. If fertilisation does not occur during the period of viability the ovum becomes surrounded by a dense albuminous envelop which is unimpregnable by sperm cells.

The behaviour and function of the cervix has been known in recent years and is most interesting. This explains many of those cases which used to pass in older days as "incompatibility" between male and female partners. As early as 1933, Seguy and Vimeux[9] suggested the existence of a chemolactic affinity of the cervical mucus towards the sperm cells. With "compatible" cervical secretion progressive and steady invasion of the mucus plug by sperm cells is the rule. In "incompatible" cases this invasion is retarded and sometimes completely prevented. So far the matter is simple enough to understand, but the story does not end there. The nature and quantity of the cervical mucus is not constant through the menstrual cycles. During each ovulation the cervical secretion becomes more abundant and altered in consistency. These rheologic properties have been the subject of considerable discussion in the present times. Clift[10] in a masterly study of the subject drew attention to two properties of the cervical mucus, *viz.*, flow-elasticity, and capacity of the fluid to be drawn into threads (spinnberkeit). A menstroscope can be used to measure the flow-elasticity of the cervical mucus. Spinnberkeit can be measured equally easily by drawing away a coverslip placed on a drop of mucus and measuring the thread produced in centimeters. Both these functions of the cervical mucus are more pronounced during ovulation and insemination when these functions are at their highest is most conducive to the occurrence of conception.

This is a part of the story of the human inquisitiveness in unmasking one of the well kept secrets of nature. Sterility in olden days was a simple subject which called for a more or less straightforward line of treatment. With the increase of human wisdom the complexities in this most primitive physiological process are gradually being revealed. We do not know all yet, but with the little knowledge we possess now, one will be right in calling human sterility a problem. The solution of which is still further than we wish it to be. Yet how very simple the process of Nature is in all those cases, where it succeeds.

[7] *Endocrinol*, **39**:262, 1946.
[8] *Am. J. Obstet & Gynec.*, **48**:75, 1944.
[9] *Gynec. et Obst.*, **27**:346, 1933.
[10] *Proc. Roy. Soc. Med.*, **39**:1, 1945.

NOTES AND NEWS

COLLEGE OF PHYSICIANS AND SURGEONS OF BOMBAY

The following candidates have been declared to have passed the Examination for the Diploma of Fellowship held in September, 1947:

Adatia, Manilal Devchandbhai; Amin, Ramanlal Purshottam; Grant, Kaiki Byram; Mistry, Maneck Rustomji; Noronha, Ligorio Nicolau Antonio Cabral de; Sheth, Sarla Laxmichand (Miss); Sheth, Uttamchand Khunchand and Udani, Sushila Prabhakar (Mrs.).

PATENT INDIAN MEDICINES

Patent or proprietary medicines in the Indian Union will have to be registered, as directed by the Drugs Control Order, with the Central Drugs Laboratory, Government of India, 110 Chittaranjan Avenue, Calcutta.

In course of a circular issued from the Central Drugs Laboratory it is pointed out that under the Drugs Act, 1940, and the Rules made thereunder all patent or proprietary medicines with undisclosed formula (*i.e.*, where a full list of all the potent or poisonous ingredients of a medicine with the exact quantities of each is not printed on the label or container of the medicine) must be registered at the Central Drugs Laboratory.

This order, however, does not affect the medicines or substances conclusively used or prepared for use in accordance with the formulae of the indigenous systems of medicine, as also patent or proprietary medicines intended to be used solely for veterinary purposes subject to this condition that the description of such medicine is given on the label or container.

It is only on the receipt of the Certificate of Registration from the Director of the Laboratory to the particular medicine submitted to him that it can be marketted. The Director of the Laboratory is authorised to reject any application for registration if the formula stated by the manufacturer does not conform to the results of the test.

A NEW ATOMIC ENERGY LABORATORY

The following account of the proposed reorganization of the Argonne National Laboratory, published in "Science" gives an idea of the vast facilities and resources needed for an up-to-date atomic energy laboratory.

The proposed laboratory will be situated 26 miles to the South-West of Chicago, Illinois. This site has been found most suitable from the consideration of geographical location, transportation facilities, the type of foundation, availability of sewage, water and power facilities. There will be some 12 large buildings to accommodate the administration, physics, biology, medical and engineering research, nuclear reactors, etc. It is expected that the whole laboratory will be completed in 3 years. For future expansions and further developments, a total area of about 3,645 acres have been acquired all round the laboratory.

Under the present arrangement about 25 participating academic and research institutes such as Chicago University, University of Illinois, Carnegie Institute, North Western University elect one representative each. This council of 25 members elect a board of 7 Governors for the laboratory who review general matters of policy and make recommendations to the Government. 3,645 acres is over five square miles. The Nuclear Energy Station will therefore have the size of a medium sized city.

LADY TATA MEMORIAL TRUST AWARD FOR 1947-48

The trustees of the Lady Tata Memorial Trust announce the award of the following Scholarships and Grants for the year 1947-48:

I. International award for research in diseases of the blood with special reference to Leukaemias are made to: Dr. Jorgen Bichel, Denmark; Dr. Pirre Cazal, France; Dr. Pierre Dustin, Belgium; Dr. Maurice Guerin, France; Dr. Simon Iversen, Denmark; Dr. Joseph Japa, Poland; Dr. Edith Paterson, Great Britain; Prof. Edorado Storti, Italy; Dr. Peter A. Gorer, England; Dr. Johannes Clemmesen, Denmark; Dr. C. F. M. Plum, Denmark; Dr. Tage Kemp, Denmark; and Dr. Guido Totterman, Finland.

II. Indian scholarships for investigations having a bearing on the alleviation of human suffering are awarded to Messrs. Suprobhat Mukerji (Chemistry), Kalyanmoy Mukerji (Physiology), Naresh Chandra Ghose (Biochemistry), of the University College of Science, Calcutta; Messrs. P. R. Gupta (Chemistry) and Yashwant Balkrishna Rangnekar (Biochemistry) of the Indian Institute of Science, Bangalore and Mr. Haridas Brahmachari (Biochemistry) of the Nagpur University, Nagpur.

NATIONAL INSTITUTE OF SCIENCES OF INDIA

At the instance of the Scientific Man-Power Committee of the Government of India the National Institute of Sciences proposes to assess the "drift" or "leakage" of scientific talent in the country. All persons, who possess scientific and technical qualifications, and are either unemployed or engaged in non-technical or unproductive occupations are requested to send full information regarding:

Name : Age : Permanent and present address : Scientific or technical qualifications and experience : present occupation : whether the qualifications possessed by the candidate are being used to best advantage in his present occupation : whether conditions of work in the present occupation can be improved and if so, how.

It is also proposed to compile under the auspices of the National Institute of Sciences of National Register of Scientific and Technical Personnel, avail-

able in India. All persons, who possess scientific, technical or engineering qualification are requested to send full information regarding :

Name : Age : Permanent and present address, qualifications and experience : Present occupation and nature of work.

This enquiry is confined to persons possessing :—B.Sc. (Hons.) or Post-Graduate Degree in Science : Diploma in Technology or Engineering : Diploma or Degree in Medicine, Agriculture, Forestry. Animal Husbandry, Veterinary and related subjects as the 'minimum' educational qualification.

Replies to this questionnaire should be sent in 'duplicate'—one addressed to Prof. S. P. Agharkar, C/o. Law College, Poona, and the other to Secretary, National Institute of Sciences of India, University Buildings, Delhi—*Hindustan Standard, Calcutta.*

INDIA'S NEED FOR MORE DOCTORS

London, Sept. 26,—Dr. S. C. Sen, Indian delegate to the World Medical Association conference held in Paris last week, said here that India and Pakistan had only 50,000 doctors, fewer than a fifth of the number required, and it was hoped the two Dominions would take immediate steps to expand medical schools.

Dr. Sen was speaking in the presence of the British Minister of Health, Mr. Bevan, at a reception given him by the Indian High Commissioner in London, Mr. Krishna Menon.

The Pakistan delegates to the conference, it was stated, had not been able to go to Paris because the situation at home demanded their presence in Karachi.

Dr. Sen said that the USA had decided to grant $50,000 a year to the new World Medical Organization formed in Paris. The first meeting of its Secretariat Council would probably be called in April or May, 1948.

He told Reuter that members of the Indian medical profession were in general agreement with the British Medical Association in their opposition to the nationalization of medicine on the grounds that the relationship between doctors and patients would be largely destroyed.—*The Statesman.*

TWO SHIFTS FOR MEDICAL COLLEGE, CALCUTTA

A recent West Bengal Govt. Press Note states: In view of the scarcity of trained medical personnel the Government of West Bengal have decided to run the Medical College in two shifts and as a result 125 more students will be admitted for the current session. The selection for the first batch has already been made and that for the second batch will be made out of the applications already received.

VILLAGE HEALTH CENTRES : WEST BENGAL GOVERNMENT SCHEME.

The establishment of a health centre consisting of an outdoor dispensary and a four-bed hospital for each of the 2,050 village unions in West Bengal is envisaged in a Government proposal to provide medical relief for people in rural areas. Of the four hospital beds, two will be set apart for maternity cases and two for emergency cases.

The scheme is estimated to cost 4,61,25,000. Of this—Rs. 3,07,50,000 will be capital expenditure and Rs. 1,52,75,000 recurring.

The staff of each centre will comprise a medical officer, an assistant, a trained midwife and two menials Apart from attending the dispensary and the hospital, the staff will take preventive measures in the locality, periodically examine the health of school children and carry on health propaganda.

Mr. A. P. Chowdhury, Finance and Public Health Minister, told Press representatives that the Government had already received two offers of Rs. 50,000 and Rs. 30,000 from the public in Midnapore district for the establishment of such centres in their respective areas.—*The Statesman,*

T. B. TREATMENT COURSE IN ASSAM

Col. A. N. Chopra, Inspector-General of Civil Hospital and Director of Public Health, Assam, has arranged for an intensive course of instruction in prevention, diagnosis, treatment and prognosis of tuberculosis.

The course will be held at the tuberculosis clinic, near the Civil Hospital, Shillong, for a fortnight from October 1. The purpose of this course is to place before the doctors the latest advances in respect of tuberculosis treatment and also to give an intensive training in routine work, so that doctors may afford more effective relief to patients suffering from tuberculosis.

Ten selected doctors from Government service will be admitted to the course. Any registered medical private practitioner interested in receiving the training will also be admitted if he gets permission from the Inspector-General of Civil Hospitals, Assam, provided the number does not become too unwieldy for imparting personal instruction.—*The Statesman.*

INTERNATIONAL MATERNITY AND CHILD WELFARE

An international conference on maternity and child welfare was held in London during the last week of June. Delegates from many European countries, including Germany, Austria, and Italy, attended, and two of the sessions were devoted to a discussion of Europe, her present needs and future outlook, in which delegates from twelve countries participated. The Minister of Health, in opening the conference, referred to the gratifying fall in infant and maternal mortality in Great Britain. In 1946, when the birth rate was the highest for over twenty years, infant mortality stood at 43 per 1,000 live births, and maternal mortality at 1·43 per 1,000 births, or less than half the figure for 1938. The stillbirth rate was about two-thirds of what it was before the war. These advances, said Mr. Bevan, had been made because the Government was trying to ensure that such resources as were

available reached those who most needed them. The improved vitality and "bonniness" of infants were also to be attributed to the higher standard of infant care brought about as a result of propaganda and the more intelligent devotion of the modern mother. He believed that still greater improvement could be effected through the planning of available resources, which was the aim of the National Health Service Act.

Mr. Bevan praised the work of voluntary organizations in this as in other fields, and said that local authorities in working out their new schemes would be wise to make use of voluntary organizations and to contribute towards their funds. Sir Wilson Jameson, Chief Medical Officer of the Ministry of Health, who presided over the ensuing session, also stressed the useful part played by voluntary organizations. "We can not do without voluntary organizations in this country", he said. "They have to be given as prominent a place in the new Health Service as they have had in the past. It would be a sad day for this country if voluntary work were to come to an end."

A discussion developed on the training of doctors and midwives. Sir Andrew Davidson, Chief Medical Officer of the Department of Health for Scotland, said that to gain adequate clinical experience for maternity and child welfare working intending practitioners in this branch of medicine should divide their time between maternity and child welfare services, especially those which had a department for breast-feeding difficulties, nurseries which catered exclusively for healthy children, and sick children's hospitals. The singleness of the mother and child as a biological unit should always be kept in mind. Lady Reading urged that medical students as part of their training should attend infant welfare centres in order to see how doctors dealt with normal children.

Nutrition of Mother and Child—In a session on nutrition Dr. H. E. Magee, adviser in this subject to the Ministry of Health, said that the national indices of the health of mother and child, which had been improving during the war, were checked in 1940-1, but since 1942 maternal, infant, and neonatal mortality rates had been falling. There was less anaemia among women and children in 1943 than in pre-war years, and there had been further improvement since then in some areas. The constructive and protective nutrient requirements of the expectant mother were almost entirely met by her rations and allowances alone, irrespective of canteen or other extra meals and the family pool, and the rations of the nursing mother and infant together provided more than enough of nutrients for both. He held that much of the improvement in the health of mother and child during and since the war as compared with pre-war years could be attributed to better diet.

Of the reports made by Continental delegates the most encouraging came from Norway. Dr. Hanna Berghoff described the work of the Norwegian Women's Nursing and Health Association, which had 200,000 members (in a country with a population of only three million) and 300 stations for maternity and child welfare spread all over the country. The latest statistics for all Norway gave an infant mortality rate of 35·5 per 1,000 live births, and in Oslo in 1945 the rate was 21·2, the lowest ever recorded. It was stated that in Austria at the present time the question of providing milk for infants is the outstanding problem. In one maternity hospital in Vienna a collecting centre for mothers' milk has been established from which the bottled milk is taken daily to the homes where it is needed.—*Brit. M. J.*, **2**:144, 1947.

ANTENATAL PEDIATRICS

At a famous children's hospital governed by a charter which limits the upper age for patients to 12 years the medical staff recently asked the board of management for permission to treat pregnant women, on the grounds that they sought thereby to influence the unborn child. This would have pleased Ballantyne, sometimes called the father of antenatal care. In his early work he wrote of attempts "to cure before birth the disorders and diseases of the foetus." This quotation was recalled by L. G. Parsons in the fifty Blackader lecture, delivered in Canada last year (*Canad. Med. A. J.*, **55**:327, 1946). Recent events and discoveries have added particular interest to the problem.

"There is considerable evidence that as a result of rationing and better distribution of food the diet of a large part of the population has improved during the war years," and after a careful analysis of all the factors concerned Parsons concludes that the stillbirth rate and the neonatal death rate have fallen in part as a result of the improved nutrition of the mothers. The diet in the last third of pregnancy is of special importance. The mother transfers not only nutrients to the fœtus but also certain immune bodies. The whole question of transferred immunity is ripe for reconsideration in the light of the estimation of serum proteins in the newborn and especially of the gamma globulin protein. Original work on this point must be interpreted with caution, because of the variations in placental structure. On the negative side, so to speak, Parsons mentioned the effects of diabetes in the mother upon the fœtus and newborn baby, and the alarming and fascinating story of rubella and fœtal deformities. Careful treatment of diabetic mothers will further reduce the risk of stillbirth, neonatal death, or gigantism, Australian investigators have suggested that pooled or adult serum should be given to the pregnant woman to confer immunity to the risks of rubella, but according to Parsons stocks are not available in this country.

In recounting the story of the rhesus factor the lecturer modestly refrains from explaining how right the Birmingham school were to insist that hæmolysis is the primary lesion and the erythroblastosis the result of blood destruction. It is sometimes argued that undue prominence has been given to the rhesus factor, but Parsons quotes Haldane to the effect that congenital hæmolytic disease is responsible for more deaths than any other inherited disease, possibly for more than all of them put together. For this reason it is wise to test the serum of every expectant mother against the Rh factor—in her own interest as well as

that of the baby. Routine Wassermann testing has already been widely accepted. Both tests have the support of obstetricians, among them Prof. F. J. Browne, who has long and wisely taught the exact value of antenatal care. The eighth edition of his little book, 'Advice to the Expectant Mother', has just appeared and celebrates its twenty-first birthday with a new short section on relaxation in pregnancy and labour. Here is antenatal pædiatrics translated for the benefit of the mother. The close co-operation now being achieved between obstetricians and pædiatricians is a good augury for the future of the young infant.—*Brit. M. J.*, **2**:182, 1947.

SUNFLOWER-SEED PROTEIN

The sunflower, though grown in this country mainly for decorative purposes, is in many parts of the world a valuable source of food. The seeds are rich in oil, which is edible and readily extracted. The residual meal contains up to 50 per cent of proteins, and should therefore be a valuable food for livestock if its constituent amino-acids are such as to endow it with a high biological value. Doubts on this point were recently expressed by Day and Levin, (*Science*, **101**:438, 1945) who concluded that sunflower meal is more important as a source of the vitamin B complex than of protein. In support of this view the biological value of the protein was found by Mitchell, Hamilton, and Beadles (*J. Nutrition*, **29**:13, 1945) to be inferior to that of the soya bean, and in the same low class as that of oats, wheat, and barley. Block and Bolling (*Arch. Biochem.*, **6**:277, 1945) however, agreed with Grau and Almquist (*Ibid*, p. 287) in claiming that the amino-acid analysis of the meal compares very favourably with that of beef muscle. Which of these conflicting views was to be believed? Experiments to clear up this point have now been reported by Grau and Almquist (*Proc. Soc. Exper. Biol. N.Y.*, **60**:373, 1945). In this work the growth rates of chicks given South American sunflower meal as a source of protein were compared with the rates of others given casein or sardine meal. As a result the sunflower meal was found to be fully equal to these excellent sources of protein. Its biological value, moreover, was not improved by adding lysine, an amino-acid which is deficient in many cereal and oil-seed proteins. When given at a level equivalent to 20 per cent of protein in the diet the sunflower meal was satisfactory as a complete source of amino-acids for the young chick.

If these results are duly confirmed the sunflower must rank high in nutritive value, particularly among vegetable foodstuffs. In a practical way its excellence has already been recognized in Soviet Russia and other parts of the world, where it is grown in large quantities. In our own country, however, its value as a possible alternative to more familiar crops must obviously depend not only on the food value per unit weight of seed but on numerous other factors, including the yield of seed per acre. Whether sunflowers deserve more attention than that already given by the backyard poultry-keeper, and could profitably take the place of other crops in well-tilled soil, is a question which only the expert agriculturist can decide. A plant which yields both oil and good quality protein, and which does not require tropical warmth or moisture for its cultivation, is, however, certainly worth intensive investigation. The plant-breeder should inquire into the possibility of evolving improved strains with larger seeds and higher oil content. The colonial administrator should not neglect the possibilities of the sunflower when faced with unpromising soil which is unsuitable for other crops.—*Brit. M. J.*, **2**:22, 1947.

VOLATILE VITAMINS

Professor M. Maisel and his collaborators at the Microbiologic Institute of the U.S.S.R. Academy of Science confirmed the hypothesis of Academicin N. Kholodny (Academy of Science of the Ukrainian S.S.R.) that in growing plants such as peas a number of volatile vitamins—thiamine, pyridoxine, nicotinic acid and para-aminobenzoic acid—are present. Coming in through air they act on micro-organisms in the same way as when added to nutritive medium in liquid or powder form. This property was discovered when vitamin contents were tested in foods.

At present volatile vitamins are added to nutritive mediums which activate the growth of micro-organisms. Some of them, as yeast and yeastlike fungi, in absence of vitamins demonstrate symptoms of avitaminosis observed as disturbance of fermentation processes, cell infiltration and others. When petri dishes with yeast cultures with and without vitamins stood side by side, volatility of vitamins could be registered by many of the aforementioned signs. If the petri dishes were placed in different rooms the volatility was not observed and signs of avitaminosis developed. This has a practical meaning, permitting the establishment of the quantity of niacin, thiamine, pyridoxine and other vitamins in food and plants even in very small quantities. —*J. A. M. A.*, **134**:392, 1947.

A CEREBRAL PALSY UNIT

The cerebral palsy unit, the first to be established in this country, set up in 1943 at Queen Mary's Hospital for Children, Carlshalton, for the treatment by the methods of Professor Phelps of Baltimore, has been treating an average of 14 children at a time. It is now proposed to enlarge the unit to take 20 at a time and later 40 and still later 60. A report by the Hospitals and Medical Services Committee of the London County Council shows that the Phelps method gives good result. Some hopelessly crippled children have been rendered capable of taking part in the life of at least a school for physical defective children and in many cases in a normal school life. The facilities for the treatment are therefore to be extended as quickly as possible. Both the Ministry of Health and the Ministry of Education want the work to be developed. The latter has appointed a technical adviser, who has visited America to study the methods employed there and the results achieved. A close

association has been developed with a new school for children suffering from cerebral palsy which has been established by a voluntary organization. The staff of the unit includes a part time consulting physician and an orthopedic surgeon.—*J. A. M. A.*, **134**:391, 1947.

J.I.M.A. SUB-EDITOR OBTAINS D.C.H.

Dr. N. G. Mojumder, M.B., a Sub-Editor of the Journal of the Indian Medical Association, now on study leave, has passed the D.C.H. examination, London.

XXIV ALL-INDIA MEDICAL CONFERENCE

The XXIV All-India Medical Conference will be held from 24th to 29th December 1947 at Bombay, in the compound of the J. J. Group of Hospitals and Grant Medical College. The Association of Physicians of India and the Association of Surgeons of India are holding their annual Conferences at the same venue at the same time.

The following is a detailed programme of the Conferences:

Pandal and Anatomy Theatre

22nd Dec. '47	9 a.m.—1 p.m. ..	Meeting of Working Committee, I.M.A.
	2-30 p.m.—5 p.m. ..	Meeting of Working Committee, I.M.A.
	5-30 p.m.—7-30 p.m.	Meeting of Working Committee, I.M.A.
23rd Dec. '47	9 a.m.—11 a.m.	Conference of Office bearers of Central & Provincial Offices.
	11-30 a.m.—1 p.m. ..	Central Council meeting.
	2-30 p.m.—5 p.m. ..	Central Council meeting.
	5-30 p.m.—7-30 p.m.	Central Council meeting.
24th Dec. '47	9 a.m.—12 noon	Inauguration of the Conference.
	12 noon—1 p.m.	Election of Subjects Committee.
	1 p.m.—3 p.m. ..	Lunch interval.
	3 p.m.—4-30 p.m.	Opening of Exhibition by the Mayor of Bombay.
	4-30 p.m.—5-30 p.m.	Tea in the Exhibion Ground.
	5-30 p.m.—7-30 p.m.	Subjects Committee Meeting.
	9 p.m.—11 p.m..	Subjects Committee Meeting.
25th Dec. '47	10-30 a.m.—1 p.m. ..	Open Session of the Conference I.M.A.
	2-30 p.m.—4 p.m. ..	Open Session of the Conference I.M.A.
	6-30 p.m.—8 p.m.	Open Session of the Conference I.M.A.
	9-30 p.m.—11-30 p.m.	Entertainment by Medical Students.
26th Dec. '47	5-15 p.m.—7-15 p.m.	Open session of the Conference.
	9 p.m. ..	Boat Trip.
27th Dec. '47	9 a.m.—12 noon	Discussion on Functional Uterine Bleeding. *President:* Mrs. Dadabhoy. *Speakers:* 1. Sir L. A. Mudaliar, 2. Dr. Bhaskar Menon, 3. Dr. M. D. Joshi (Radio) and 4. Dr. R. E. Sethna (X-Ray).
28th Dec. '47	2-30 p.m.—4 p.m. .. } 4-30 p.m.—6 p.m. .. }	Scientific Papers.
	9 a.m.—12 noon	Discussion on Antibiotics. *President:* Dr. Erulkar. *Speakers:* Col. Amirchand (Medicine), Dr. Baliga (Surgery), Dr. Rajan (Venereology) and Dr. Rebelo (Dermatology).
	9 p.m. ..	Subscription Dinner.
29th Dec. '47	9 a.m.—12 noon	Discussion on Appendicitis. *Speakers:* Dr. Pandalai (Diagnosis), Dr. Moolgaonkar (Treatment), Dr. Wig, Punjab (Medical Aspects) and Dr. Deboo (Radiological Aspects).
	2-30 p.m.—5-30 p.m.	Scientific papers.
	6 p.m.—7 p.m. ..	Joint Concluding Session.

Evening is Free for Private Entertainments.

30th Dec. '47	9 a.m.—12 noon	Scientific papers or Trip to Caves.

CONFERENCE OF ASSOCIATION OF PHYSICIAN OF INDIA

Pathology Theatre.

26th Dec. '47	11-15 a.m.—12-45 p.m.	Inauguration of the Conference.
	12-45 p.m.—1-15 p.m.	Business meeting of the Governing Body.
	2-30 p.m.—4-30 p.m.	Scientific papers.
	5 p.m.—6 p.m. ..	" "
	9 p.m. ..	Boat Trip.
27th Dec. '47	12 noon—1 p.m. ..	Business Meeting.
	2-30 p.m.—4-30 p.m.	Scientific papers.
	5 p.m.—6 p.m.	" "
	8-30 p.m. ..	Subscription Dinner.

CONFERENCE OF THE ASSOCIATION OF SURGEONS OF INDIA.

Physiology Theatre.

26th Dec. '47	9 a.m.—10-30 a.m.	Inauguration of the Conference by Hon. Dr. Gilder, Minister of Health, Govt. of Bombay.
	2 p.m.—5 p.m. ..	Discussion of Bone Tumour.
	9 p.m. ..	Boat Trip.
27th Dec. '47	2 p.m.—5 p.m. ..	Discussion on Special Treatment.
	8-30 p.m. ..	Subscription Dinner.
28th Dec. '47	2 p.m.—5 p.m.	Discussion Burns.
	9-30 p.m.—11-30 p.m.	Entertainment.
29th Dec. '47	2 p.m.—5 p.m. ..	General body meeting.
	6 p.m.—7 p.m. ..	Joint Concluding Session.

Morning programme on the first 3 days will be visits to different hospitals to see clinical and operative work.